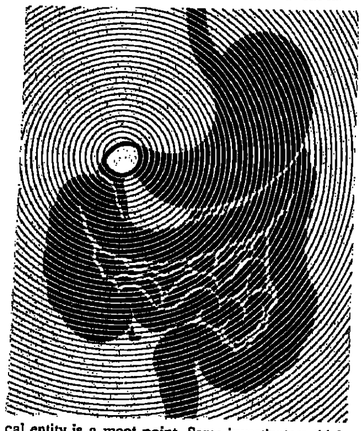
G.I. FORUM

ROCHE

A CURRENT REVIEW OF INVESTIGATIONS IN GASTROENTEROLOGY

Intestinal hotspot

Duodenitis may be observed by histological examination,[1] through endoscopy[2] and can often be determined by careful interpretation of x-ray findings.[3] But whether chronic duodenitis exists as a clear-cut clinical entity is a moot point. Some investigators think so.[4] Others are skeptical, noting that symptoms of duodenitis may be indistinguishable from those of peptic ulcer.[5] One of the doubters[1] believes that primary nonspecific duodenitis seldom explains symptomatic illness but rather is a secondary manifestation of certain other diseases, or is a coincidental finding. He notes that a source of confusion to clinicians is disagreement among radiologists as to whether a certain pattern of muscular irritability in the duodenum can be interpreted as mucosal inflammation.[1]



Duodenitis—a matter of definition

This uncertainty about the identification of duodenitis, one group observes, may be partly due to the fact that previous studies evaluated only specific criteria in defining the disease.[4] These workers, when correlating four criteria (clinical evaluation, gastric secretion, radiologic and histologic findings), were able to distinguish a group of patients who differed from normal controls, patients with functional dyspepsia, and duodenal ulcer patients. Their findings lent support to the concept of "chronic duodenitis" as a clinical disease entity, but the authors did not deny that it might represent an early stage of duodenal ulcer.[4]

Hotbed of duodenal ulcer?

Does nonspecific duodenitis precede peptic ulcer? This point is still unsettled. Some hold that it could be an intermediary step in the pathogenesis of ulcer or in the process of ulcer healing.[3] They consider such a concept—which would account for many symptoms previously attributed to ulceration—useful in dealing with recurrent dyspepsia. Other experts,[6,7] however, feel that true duodenitis is not an early stage of ulcer. They[6] point out that the normal state of the mucosa in areas of the duodenum other than the ulcer site makes it unlikely that there was a preexisting diffuse inflammatory process.

Duodenum—target for trouble

A general or localized inflammation of the duodenum may result secondarily by extension of disease in contiguous organs such as the colon, pancreas, gallbladder, liver or adrenals.[5] Or it could result from local factors such as chronic passive congestion or from duodenal stasis. Some degree of chronic inflammation of the duodenal mucosa may result from stasis of the food column inside a duodenum plagued by delayed motility. The duodenum, located in an unusually vulnerable part of the abdomen, is in contact with the largest abdominal blood vessels, is the collecting point for intestinal lymph, and is the center for the gastrointestinal autonomic nervous system.[1]

Which came first, the inflammation or the acid?

After the 1920's, interest in duodenitis was overshadowed by interest in gastric hypersecretion as related to ulcer.[3] Duodenal ulcer patients are usually hypersecretors. In fact, some investigators believe that hyperchlorhydria, duodenitis and duodenal ulcer are different stages of the peptic ulcer diathesis and that hypersecretors represent a reservoir of persons who may develop peptic ulcer at times of emotional stress or upon exposure to provocative agents.[3] But dissenters[4] note that duodenal inflammation could result from a nonspecific cause such as decreased mucosal resistance, which then leads to ulceration.

Treat like ulcer

Duodenitis patients have symptoms mimicking peptic ulcer. Epigastric pains relieved by food intake and antacid occur in duodenitis.[4] Hunger, gnawing or burning pain present in the same manner and rhythm as in ulcer, so that the pain of duodenitis is relieved by milk, food or antacids just as in ulcer. *Therapy* for patients with suspected duodenitis resembles that for peptic ulcer and response may be exactly the same.[5]

References: 1. Palmer, E. D.: *Clinical Gastroenterology*, ed. 2, New York, Harper & Row, 1963, pp. 192-202. 2. Bréber, J. P.: *Gastroenterology*, *61*:55, 1971. 3. Ostrow, J. D., and Resnick, R. H.: *Ann. Intern. Med.*, *5*:1303, 1959. 4. Beck, I. T., *et al.*: *Gut*, *6*:376, 1965. 5. Wechsler, R.: "Duodenitis," in Bockus, H. L. (ed.): *Gastroenterology*, ed. 2, Philadelphia, W. B. Saunders Co., 1964, vol. 2, pp. 119-124. 6. Chait, R.: *Digestion*, *1*:175, 1968. 7. Bockus, H. L. (ed): *Gastroenterology*, ed. 2, Philadelphia, W. B. Saunders Co. 1964, vol. 2, p. 112.

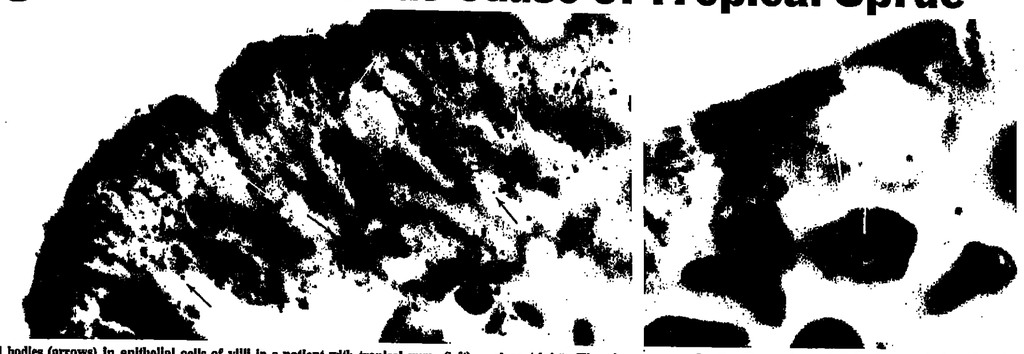
Medical Tribune

©1973, Medical Tribune, Inc.

and Medical News

Vol. 14, No. 24 — *world news of medicine and its practice—fast, accurate, complete* — Wednesday, June 27, 1973

Algae Are Identified as Cause of Tropical Sprue



Paired bodies (arrows) in epithelial cells of villi in a patient with tropical sprue (left). Similar paired bodies in biopsied villi of physician volunteer 20 days after ingestion of algae (right). The six-year tests by the Bronx team led to the conclusion that the pathogen in sprue is apparently the zygote form of the alga Prototheca portoricensis.

Medical Tribune Report

NEW YORK—Is tropical sprue an algal disease of man?

The likelihood is very high, according to a Bronx team that reported the first clinical and pathologic evidence linking the disease to ingestion of a specific algal subculture.

The data were described here by Dr. Leslie H. Bernstein, director of gastroenterology at Montefiore Hospital and Medical Center, who detailed the six-year series of research studies leading to the finding that the pathogen in sprue is apparently the zygote form of the alga Prototheca portoricensis. His collaborator was Dr. Harold Lepow, director of pathology at Lincoln Hospital. Both Montefiore and Lincoln are teaching facilities of Albert Einstein College of Medicine.

Continued on page 12

Exclusive Tribune Interview

Food Is an Insufficient Source Of Vitamin C, Pauling Asserts

He Suggests That FDA Introduce Teaching Plans on Nutrition

Decries Lack of Information On Amounts Needed in Diet

In this issue MEDICAL TRIBUNE continues its extensive and exclusive interview with Nobel Prize winner Linus Pauling, Ph.D., concerning his views of vitamin C and the struggles that have surrounded and often censored them. His best-selling book, *Vitamin C and the Common Cold*, has upset traditional views of nutrition in medical circles.

In combating censorship and criticism of his views, Dr. Pauling has ranged from the halls of the National Academy of Sciences to TV talk shows. He has particularly attacked *Medical Letter* for what he considers serious distortions of his views. Since December, 1970, when his book was first published by W. H. Freeman and Company, studies from Europe and Canada have increasingly confirmed his views on vitamin C and the common cold and

Continued on page 29

Text of interview with Dr. Pauling:

Q. Professor Pauling, all physicians are taught that food is the best source of vitamins and a balanced diet provides vitamin adequacy.

A. Well, that is wrong. You can't get the amounts of vitamin C you need in foods. It is essentially impossible. The proper amount of ascorbic acid that leads to the best health is of the order of grams per day for a person, for most people.

Q. What dosage of ascorbic acid do you take?

A. I have been taking 6 Gm. a day. I was taking 3 Gm. a day for six years. I decided to go to 6 Gm. a day, and it seemed to me that my health was better with high intake.

Q. Couldn't you get ascorbic acid adequacy with very rich source foods?

Continued on page 29

INSIDE THIS ISSUE

Australian Nobelist, 73, Carries Card: Spare Me Any Heroic Measures

Medical Tribune World Service

MELBOURNE, AUSTRALIA—Sir Macfarlane Burnet, the 73-year-old Nobelist, carries a card in his wallet that says:

"I request that, in view of my age, any prolonged unconsciousness, whether due to accident, heart attack, or stroke, should be allowed to take its course without benefit of an intensive care or resuscitation ward."

He explained: "Once I reach the stage of pre-death, all I ask is that I go on to the end with as much dignity and as little pain as possible. Death in the old should be accepted as something always inevitable and sometimes positively desirable. Physicians should not compel old people to die more than once."

Sir Macfarlane said that modern medical science had become too successful in its ability to prolong life.

Continued on page 12

Ca Cells Reported Readily Observed In Urine Sediment

Medical Tribune Report

NEW YORK—Malignant cells of urothelial origin can be readily observed in the unstained urinary sediment of patients with transitional cell carcinoma, making possible an early diagnosis of malignancy, a Boston urologist reported here.

With "very little" training even those who are not technologists can learn to recognize the characteristics of these malignant cells, Dr. Joseph F. Sherer, Jr., Associate Professor of Urology at the University of Massachusetts, told the 63rd annual meeting of the American Urological Association.

The urologist can thus be immediately alerted to the possibility of urothelial malignancy, and a confirmatory diagnosis

Continued on page 12

Two typical malignant transitional cells seen in urinary sediment of a patient show enlarged nuclei crowding the cytoplasm.

Editorial

For a Free Scientific Press

WHAT DO GOOD WINES and good scientific opinions have in common? If you collect wines, you know that a great Bordeaux gets greater with age. A lighter wine, particularly one of the mediocre whites, improves for a short while and then goes bad, and a bubbly champagne can give you a good froth but after a limited life span goes real bad. Since this principle also holds for both research or basic ideas in medicine, there is much that we write that is put aside. If it is mainly froth, one is glad it wasn't published. If its body has substance, it may become even more pertinent. If it's really good, it stands the test of time.

About a year and a half ago we were upset by the debasement of medical debate. Outstanding instances were attacks

Continued on page 11

Coronary Disorder, Hypertension Shown In Obese Subjects

Medical Tribune World Service
From West German Edition

LEIPZIG, EAST GERMANY—A study of 1,000 obese subjects disclosed that 173 showed signs of hypertension and 524 suffered coronary insufficiency, Dr. I. Hunecke, of Karl Marx University, reported here at the eighth Congress for Internists. Coronary insufficiency was found in 71 per cent of the hypertensives. The subjects included 752 women and 248 men between the ages of 18 and 60.

Of the 173 persons with signs of hypertension, 54 per cent were in stage I (WHO definition), 27 per cent in stage 2, and 19 per cent in stage 3, Dr. Hunecke said.

WHO has proposed the following categories of blood pressure: potential hypertension—a family history of high blood pressure; borderline hypertension—140-160 systolic, 90-95 diastolic; moderate hypertension—160-180 systolic and/or 95-115 diastolic; and marked hypertension—above 180 systolic and above 115 diastolic.

Linked to Age, Obesity

A correlation between the presence of hypertension and the age and degree of obesity of the subject was noted, the investigator said. Whereas among the 18-to-20-year-olds, 10 per cent showed signs of definite hypertension, the proportion among the 51-to-60-year-olds was 36 per cent. When the subjects were classified according to degree of obesity, 11 per cent of hypertensives were found among those with 10 per cent excess weight, but 51 per cent were found in the group with 50 per cent excess weight.

Similarly, there was a definite relationship between the presence of coronary insufficiency and the subject's age and the extent of his obesity. The investigators found 15 per cent among the 18-to-20-year-olds and 82 per cent among the 51-to-60-years-old, and 49 per cent among subjects with a 10 per cent excess of weight and 62 per cent among those with a 50 per cent excess of weight.

■

Japan to Put Greater Emphasis On Clinical Training in Schools

Medical Tribune World Service

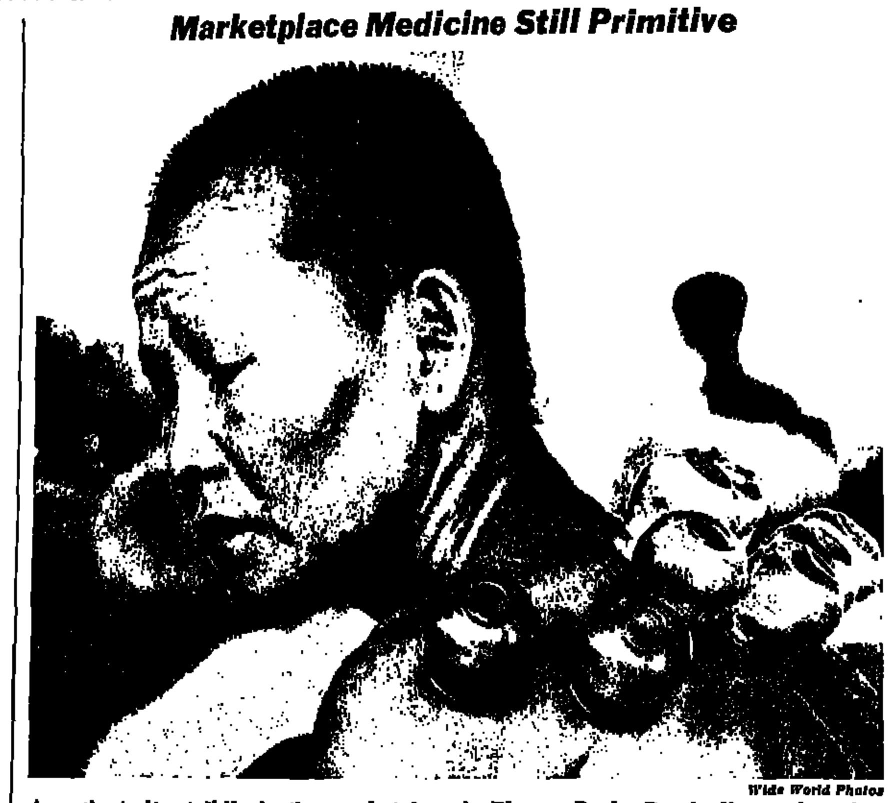
TOKYO—Medical education patterns are being altered in Japan to place greater emphasis on clinical training.

Until now the system has resembled the German method, with stress on theoretical study, and clinical education has been conducted exclusively at hospitals attached to universities.

The new policy is a move toward U.S. methods. Large general hospitals will conduct clinical training, not only for interns but also for medical students.

Government subsidies will help six university medical schools to carry out the new policy.

Marketplace Medicine Still Primitive



Wide World Photos

A patient sits stolidly in the marketplace in Phnom Penh, Cambodia, undergoing treatment at the hands of a marketplace "doctor." The treatment entails the application of heated suction cups to the back of a person suffering almost any minor ailment and is still a very popular therapy in parts of Asia.

Advances Reported in Study Of Venom in Three Snakes

Medical Tribune World Service

TEL-AVIV, ISRAEL — Two laboratory achievements in dealing with snakebite have been reported by teams at the Sackler School of Medicine, Tel-Aviv University, and Rogoff-Wellcome Medical Research Institute, Petah-Tikva.

Dr. A. de Vries told the first International Health Conference here that the results were based largely on research studies with the venom of Israel's two most important local species of snake, Vipera palestinae (VP) and Echis coloratus, and the cobra.

The investigators were able to increase the antigenicity of the VP neurotoxin by binding it to a carrier, carboxymethyl cellulose. When horses previously immunized with whole VP venom received boosters of this carrier-bound neurotoxin, antisera were obtained that, besides being strongly antihemorrhagic, increased the antineurotoxin potency, Dr. de Vries reported.

A second finding was that pepsin treatment of 6.8S immunoglobulin-G isolated from the anti-VP serum resulted in a 4.68S fragment that had the same neutralizing activity as the untreated 6.8S globulin but fewer antigenic determinants, so possibly decreasing the risk of serum reaction.

■

Cigarette Ad Curb Set

Medical Tribune World Service

AUCKLAND, NEW ZEALAND — Cigarette manufacturers have signed a three-year voluntary agreement with the New Zealand Government to restrict the size of their newspaper advertising. In addition, each cigarette pack will carry a warning about smoking health hazards similar to that on American packs.

■

Estrogen Benefits Noted In Menopause, but Study Of Longer Use Is Needed

Medical Tribune World Service

GENEVA, SWITZERLAND—Estrogen therapy can be beneficial around the time of the menopause and as women grow older, but adequate information is lacking about the effects of prolonged treatment, Dr. A. Netter, of the Hôpital Necker, Paris, told a symposium here on aging and estrogens.

Aging and the menopause, he observed, are essentially modern problems that have appeared as the life expectancy of newborn girls has increased.

"The menopause is a human problem," he said, "and we can expect to gain nothing from experiments in animals because the menopause does not exist in animal species."

Cancer Linked to High Doses

On the relationship between estrogen therapy and cancer, Dr. Netter said: "We agree with Burch and Boyd that there is no evidence that estrogens induce carcinoma of the breast in humans at the dose levels used in the management of the climacteric. We have to remember, however, that such a possibility is not excluded when using much higher doses and when using stilbestrol derivatives."

He also noted that mammary cancer seems to be much more frequent in men treated with high doses of estrogens for prostate cancer than in other men.

Although one might expect, on the basis of theoretical considerations, an increase in cancer of the endometrium after prolonged estrogen therapy, there is no evidence that this is so, Dr. Netter remarked.

■

Infant Death Rates in Europe Show Sharp Decline Since 1950

Medical Tribune World Service

GENEVA, SWITZERLAND—Infant mortality has shown a "spectacular" decrease in Europe, the World Health Organization reports, with deaths falling from 108 first-year deaths per 1,000 live births in 1950 to 34.3 in 1969. The rate fell in Yugoslavia from 118.6 to 58.6; France 51 to 19.6; Switzerland 31.2 to 15.4. In Sweden, the rate fell to 13.1, the world's lowest figure. Elsewhere, however, infant deaths are high: Pakistan, 130 and Chile, 91.6 per 1,000 live births.

■

Genetic Basis of Psoriasis Gains Support

Medical Tribune World Service

MELBOURNE, AUSTRALIA — Further evidence for the view that psoriasis has a partly genetic basis was reported here by a U.S. authority at an international symposium organized by the Australian College of Dermatologists.

Dr. Eugene Farber, head of the Department of Dermatology at Stanford University School of Medicine, said that in one study HLA antigens of 100 normal persons and 86 psoriatics were typed by Dr. Rose Payne, of Stanford's Department of Medicine. Of the normals, 20 per cent possessed HLA-12, 4 per cent HLA-13, and 7 per cent the antigen W 17. On the other hand, of the psoriatics, 21 per cent possessed HLA-12, 12 per cent HLA-13, and 34 per cent W 17.

Incidence Confirmed by Others

The high incidence of W-17 and HLA-13 has been confirmed by two other groups and seems statistically incontrovertible, Dr. Farber observed.

In discussion, he also pointed to the remarkable absence of psoriasis in Venezuelan Indians as evidence of a genetic basis.

He stressed, however, that his studies in Africa indicate that genetics is not the only operative factor. In fact, when genetically rather similar types of people are epidemiologically examined in Africa, Dr. Farber said, it turns out that great regional variation in psoriasis incidence appears, suggesting an important environmental influence. Relative humidity is one variable that could be of importance, he noted.

NEWS INDEX

CLINICAL NEWS NOTE: *"The ability of the arteriogram to demonstrate the primary tumor . . . makes this modality most useful for preoperative assessment and staging of renal neoplasms." (Dr. Erich K. Lang; see page 8.)*

FEATURE INDEX

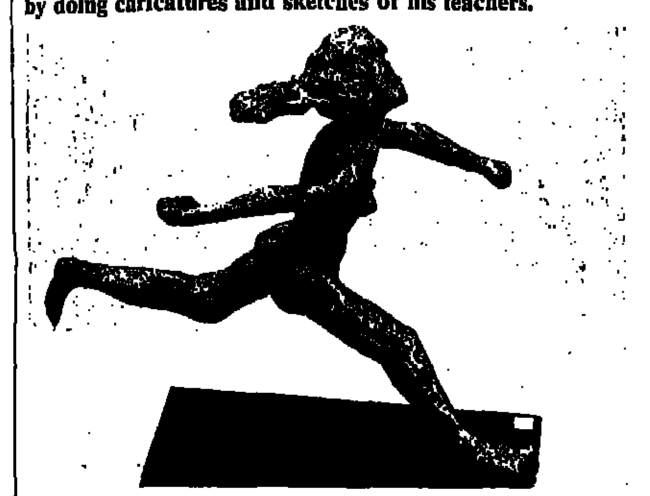
MEDICAL TRIBUNE is published each Wednesday except on Jan. 31, May 30, Aug. 29, and Oct. 31, by Medical Tribune, Inc., 880 Third Ave., New York, N.Y., 10022. Controlled circulation postage paid at Farmingdale, N.Y., 11735. Subscription $12.50, Students, $7.50.

Surgeon Mixes Art and Medicine

Dr. Nathan (above) never had more than a few rudimentary drawing classes in high school. He first began his art work by doing caricatures and sketches of his teachers.

DR. HELMUT NATHAN, president of the American Physicians' Art Association, surgeon, sculptor, and painter, has been honored with a one-man show of his work at C. W. Post College. Dr. Nathan, who is Professor Emeritus of Surgery, Anatomy, and Medical History at the Albert Einstein College of Medicine and Professor Emeritus at the University of Hamburg, West Germany, has not only published 85 scientific papers but also won prizes for his art work.

Medical Tribune Photo—Harvey Shuman



In 1964 Dr. Nathan, while recovering from a myocardial infarct, began sculpting with clay. He is currently writing a book on art and medicine and a monograph on diagnoses based on famous paintings.

New Drug Cuts Triglyceride, Uric Acid Levels

Medical Tribune Report

NEW ORLEANS—Marked reduction in serum triglyceride and serum uric acid levels, with little change in serum cholesterol, has been reported in patients with hypertriglyceridemia after long-term treatment with halofenate.

Halofenate, or MK-185—2-acetamidoethyl (p-chlorophenyl) (m-trifluoromethylphenoxy) acetate—is an investigative hypolipidemic and uricosuric agent that is administered in single daily doses.

Dr. Wilbert S. Aronow, of the Long Beach (Calif.) Veterans Administration Hospital, said that 23 patients, aged from 40 to 61 years, received 1 Gm. halofenate daily, while 25 patients, aged 39 to 65, received placebo during a 48-week period.

All patients had hypertriglyceridemia, including 35 with documented heart disease, three of whom had gouty arthritis. The patients had either type 3, 4, or 5 or nondefinitive lipoprotein patterns.

Placed on Appropriate Diet

Before treatment all patients were placed on an appropriate diet for their hypertriglyceridemia and were taken off any hypolipidemic medication. After one month of this dietary regimen and a control period of two months, patients were randomized to either halofenate or placebo for the double-blind study.

Five of the 48 patients—four on placebo and one on halofenate—died of acute myocardial infarction during the 14-month study. One patient dropped out of the study. The remaining 42 completed it.

Dr. Aronow presented these results at the 74th annual meeting of the American Society of Clinical Pharmacology and Therapeutics:

In the placebo group there was a mean increase in serum triglyceride level of 12 per cent during weeks two through 12, of 9 per cent during weeks 16 through 24, of 34 per cent during weeks 28 through 36, and of 61 per cent during weeks 40 through 48. The mean increase from control period levels was 29 per cent.

In the halofenate group there was a mean decrease in serum triglyceride of 22 per cent during weeks two through 12, of 17 per cent during weeks 16 through 24, of 17 per cent during weeks 28 through 36, and of 23 per cent during weeks 40 through 48. The mean decrease was 20 per cent.

Neither halofenate nor placebo resulted in a significant change in mean serum cholesterol level from the control period through the end of the medication period.

There was an insignificant mean decrease in serum uric acid level from the control period of 3 per cent during weeks two through 48 on placebo, whereas in the halofenate group there was a mean decrease of 38 per cent.

None of the 48 patients, including the three with a history of gouty arthritis who were in the halofenate group, developed any arthritis or renal calculi during the study.

In a few patients halofenate caused mild transient elevation of SGOT, SGPT, or CPK levels, unassociated with any symptoms or signs of muscle or liver damage. It did not cause any visual abnormalities or any other clinical abnormalities.

Dr. Aronow's co-workers were Drs. Phillip Harding, Mohammed Khursheed, Jack Vangrow, Nicholas Papageorges, and James Mays.

Hepatitis Said to Be Common With Hong Kong Flu Strain

Medical Tribune Report

SAN FRANCISCO—Hepatitis may be a not uncommon finding in patients with A2, or Hong Kong, influenza, a New York physician reported here.

Dr. Ilya Spigland told the American Pediatric Society and the Society for Pediatric Research that although influenza has been widely studied, most attention has been focused on the respiratory impairment and little mention has been made of infection with hepatitis.

A review of 24 influenza patients in Bronx Hospital during the A2 epidemic of 1972 showed, however, that eight had both clinical and laboratory manifestations of hepatitis, Dr. Spigland said.

Antigen Tests Negative

The influenza was documented by either isolation of the virus or antigen response. Tests with hepatitis antigen were negative.

Three juvenile patients developed jaundice, hepatomegaly, and elevated bilirubin and had abnormal liver function tests following an acute attack of influenza. Five adult patients had acute respiratory problems in addition to the hepatitis, and two of these had the neurologic manifestations of encephalitis as well.

In five of the patients, the jaundice was severe enough for hospital admission, and in three the liver impairment was confirmed by laboratory findings.

The majority had the respiratory and muscular manifestations and the fever typical of influenza, as well as the hepatic invasion, Dr. Spigland said. All of the patients recovered with complete regression of the clinical and biochemical signs of the disease.

Dr. Spigland commented that the large number with hepatic invasion was an unusual finding. Whether the affliction was due to the infective agent or to an abnormal host response was not clear, he said, adding that the cytotoxic effects of virus on liver cells in animals has been documented.

Carcinogens in Gasoline

Medical Tribune World Service

TOKYO—Six carcinogenic substances, in addition to 3,4-benzpyrene, have been identified in gasoline sold in Japan, according to the Ministry of Labour. The six, all aromatic hydrocarbons, are benzo-B-fluoranthene, benzo-A-anthracene, benzo-GH-terylene, chrysene, fluoranthene, and pyrene.

Reassurance Risky

Breach of Pact New Legal Peril For Physicians

Medical Tribune Report

SAN FRANCISCO—Breach of contract may be added to malpractice and lack of informed consent as a potential legal problem arising from the doctor-patient relationship, if a recent Michigan Supreme Court decision is upheld.

Dr. Jerry Zaslow, president of the medical staff of Rolling Hill Hospital, Philadelphia, told the annual meeting of the American College of Legal Medicine here that the decision in the case of Guilmet v. Campbell could seriously influence the type of reassurance a physician gives his patient prior to treatment.

"Much of what the physician says is to instill confidence and allay fears," he said, but the physician may be reluctant to give reassurance if there is a likelihood that the patient will turn on him when the result is not satisfactory.

Relationship Called Contractual

The Michigan Supreme Court held that the relationship between the patient and the physician is contractual and relies on cases related to the usual type of contract for business transactions, Dr. Zaslow recounted. The court failed to accept the concept that the mental status of the patient is part of the preoperative preparation.

The Guilmet v. Campbell case revolved around a preoperative conversation in which, according to the patient, the surgeon guaranteed the results of an operation.

A series of postoperative complications led to further surgery and a prolonged convalescence. The patient brought charges of negligence and breach of contract.

At the trial the jury found no evidence of negligence but found for the plaintiff on the assumpsit count. The decision was upheld by the Michigan Supreme Court—with one dissenting opinion that there could be no breach of contract without negligence.

Problem May Occur Again

Dr. Zaslow commented: "There is little doubt the problem will rise again, and it is not inconceivable breach of contract will be added to negligence and lack of informed consent by dissatisfied patients."

In theory, breach of contract is not malpractice, and so, technically, it is not covered by malpractice insurance, he warned. Consequently, an adverse decision would have to be satisfied by the physician.

Dr. Zaslow suggested that physicians might protect themselves from breach of contract charges by developing a form, similar to the consent form, stating that the physician will give his best efforts to the care and treatment of the patient but will not guarantee a specific outcome. The form should be signed by both parties, he said.

"No matter how repugnant the idea [of such a form] is, we must adopt a realistic attitude," he said.

"We hope that other courts adopt the minority opinion that there can not be a breach of contract without negligence," he added.

ECTOPIC BEAT

"PROOFREADERS
TIME-LIFE BOOKS
"Openings for experienced proofreaders, Monday thru Friday, 10AM to 6PM with occassional overtime. . . ."
—advertisement in the *New York Times.*

But don't bring any references from the *Times.*

(Regular beat: Immaterin Medica, page 35.)

Test Gauges Effectiveness of Treatment of Some Cancers

Medical Tribune Report

BALTIMORE—Physicians may be able to monitor the effectiveness of treatment for certain cancers more precisely with a serum alpha-fetoprotein assay developed at the National Cancer Institute, the seventh Miles International Symposium was told here.

The method may also find limited use in the detection of cancer, the report said, noting that alpha-fetoprotein (AFP) occurs at elevated levels in few diseases other than cancer.

The method was developed by Dr. Thomas A. Waldmann, of the NCI Metabolism Branch, and Dr. K. Robert McIntire, of the NCI Laboratory of Biology. Dr. Waldmann presented results of clinical studies of the detection procedure.

The technique, double antibody radioimmunoassay, can measure concentrations of the cancer-related protein at levels 1,000 times smaller than detectable with other tests usually used for the protein, he said, and consequenly can detect cancer in patients who would have appeared cancer-free in other tests for AFP.

Dr. Waldmann and Dr. McIntire found that AFP levels were elevated in the serum of 95 of 130 patients (73 per cent) with liver cancer, and in 63 of 79 patients (80 per cent) with testicular cancer. Of the latter 63 patients, three-fourths had AFP levels between 40 and 3,000 nanograms per milliliter, the smallest concentration detectable by conventional tests, the report said.

It also said that AFP levels above 40 nanograms per milliliter were detected in 10 of 46 patients (22 per cent) with pancreatic cancer, 17 of 100 with gastric cancer, 10 of 149 (7 per cent) with lung cancer, and nine of 189 patients (4.6 per cent) with colon cancer.

Not Useful for Other Types

Because AFP occurs at high levels in relatively few patients with cancers other than liver and testicular cancers, testing for this protein would probably not be useful in detecting other cancers, Dr. Waldmann commented. He suggested, however, that other cancers may be detected more frequently if tests are run for several markers. For example, he said, detection of gastrointestinal cancers can be improved by testing for both AFP and carcinoembryonic antigen.

He is able to detect liver or testicular cancer in greater percentage of patients by using the double antibody radioimmunoassay for human chorionic gonadotropin as well as for AFP, he noted.

The new test for AFP, Dr. Waldmann said, may find its most immediate application in giving physicians a measure of progress during cancer treatment. In studies of 15 patients to date, Dr. Waldmann and Dr. McIntire found that the level of AFP will drop rapidly after surgery, for example, but will not decrease below the 40 nanograms-per-milliliter level if some cancer cells remain in the patient. If cancer cells remain and resume their spread, the level of AFP begins to rise again, indicating in advance of any other signs or tests the need for further treatment.

The scientists also have found that the likelihood of detecting a recurrence of cancer after treatment is increased by measuring two or more markers.

They have come across no instances of elevated AFP among 200 healthy subjects and slightly elevated AFP levels in just two of 300 patients with chronic, nonliver diseases.

Elevated AFP levels present a problem only with respect to liver diseases, the report said. In preliminary results, elevated levels of AFP were found in approximately 25 per cent of patients with infectious hepatitis or subacute hepatic necrosis and in a few patients with cirrhosis.

Dr. Waldmann suggested that patients should be tested for hepatitis or pregnancy before being given an AFP test for cancer.

Kindergarten, Gym Programs Used To Rehabilitate CO-Poisoned Miners

Medical Tribune World Service

VANCOUVER, B.C.—A program incorporating a kindergarten approach and gymnastics was credited with a high degree of success in rehabilitating brain-damaged victims of a Japanese coal mine disaster.

Dr. Goro Yasukochi, neuropsychiatrist of the Ohmuta (Japan) Labor Accident Hospital, reported here that 180 of 200 patients who had been poisoned by carbon monoxide and suffered some degree of brain damage have returned to their original or modified work as a result of the program. He spoke at an International Symposium on the Rehabilitation of the Industrially Disabled here.

He related that after the CO-poisoned workers regained consciousness, most went through a considerable period of lack of spontaneity.

"They were either excessively or unnecessarily dependent upon the help of other persons in daily living," he said. "Such patients should be left to themselves as much as possible in the hope that this will stimulate self-adaptation."

Self-Reliance Encouraged

The Ohmuta victims were encouraged to dress themselves, to make their own beds, to wash their own clothes, and to keep their ward tidy. Meals were taken in the self-service dining room. Energetic retraining was given by a speech therapist and an occupational therapist.

Child education equipment and techniques, such as shape-matching puzzles, figure coloring, building blocks, paper folding, and clay work, proved useful. A gymnastic program was also provided.

Today all but 20 of the victims have left the hospital, and it is hoped that in time at least 15 of the remaining patients will return to work, Dr. Yasukochi said.

Lymphoid Leukemia Of Two Distinct Types

Medical Tribune Report

BUFFALO, N.Y.—Acute lymphocytic leukemia and chronic lymphocytic leukemia should be considered separate diseases because they arise from two distinct body cells, according to studies performed at Roswell Park Memorial Institute here.

Dr. Jun Minowada, principal research scientist, reported that, using new isolation procedures, he and associates have been able to classify lymphocytic leukemia into two categories—the T cell (thymus-dependent) and B cell (thymus-independent). It was found that acute lymphocytic leukemia affects cells associated with the T-cell group exclusively, while chronic lymphocytic leukemia is of the B-cell type.

Dr. Minowada commented: "Insight into the origin of the disease may be gained from this information. Both T and B lymphocytes are derived from bone marrow but subsequently go independent pathways to differentiate."

Coinvestigators were Drs. T. Han, T. Ohnuma, H. Ciudad, L. Sinks, and S. Srivastava.

Physician Ratio Improves

Medical Tribune World Service

TEL AVIV, ISRAEL—The physician-population ratio in Israel is steadily improving, and there is now one doctor for every 377 persons, according to the Ministry of Health. This compares with 436 in 1970 and 423 in 1971.

IN CONSULTATION

What's new and important in psychotherapy?

The Consultant

DR. JANICE NORTON KAUFMAN
Professor, Department of Psychiatry, University of Colorado, Denver.

INCREASINGLY in recent years the field of psychotherapy is responding to social and political pressure to provide more treatment for more people. This is a part of the broader demand for better and more equitable delivery of health care services, a trend which will probably soon find expression in some form of national health insurance. It is already making itself felt in changes in medical school curricula and specialty training generally, all in the direction of shortening training, increasing the number of physicians, and training paramedical personnel.

Psychiatry has responded with a proliferation of psychotherapies to try to answer the need—i.e., wide varieties of group psychotherapies and individual therapies of short and specific nature, such as crisis intervention and behavior therapies. There are also increased efforts to train more mental health workers and to experiment with different models for training new kinds of workers as in the community mental health centers. None of this is particularly new; there is simply much more of it. Currently, the scene is a bit chaotic generally, though the increasing excellence of crisis intervention centers is beginning to emerge. A great deal that is useful may evolve from the profusion of treatment methods. At the same time, psychiatry may be forced to better define its areas of usefulness and expertise. People and their problems have not changed appreciably, although the social setting is undergoing rapid change. Psychiatry does not yet have any strikingly new applicable information about mental illness. Recent advances in research into the neurochemistry and genetics of schizophrenia and depression are promising, but we are not yet in the position of having a genuinely etiologic method of treatment for psychoses.

"...Psychiatry may be forced to better define its areas of usefulness and expertise."

Psychoanalytically oriented individual and group psychotherapy currently may not appear as useful as in the past because they involve more knowledge and more training and because there are built-in limitations in available time and trained personnel. I think, however, they have stood the test of time as the best available treatment for nonpsychotic patients. I hope we do not overlook this in our need to respond to the very real social pressures we live with. I also hope we continue with research and evaluation of all psychotherapy. Our knowledge is not yet great enough to apply mass methods to individual problems in a field which involves everything from inborn genetic differences to faulty learning and general human unhappiness.

Did psychotropic drugs change the status of psychoanalysis?

I do not believe either the advent of psychotropic drugs or the current proliferation of psychotherapies has changed the status of psychoanalysis. Despite its shortcomings, psychoanalytic theory remains the best theory of human behavior, both normal and pathological, we yet have. Many of the psychotherapies currently in vogue are heavily dependent on the psychoanalytic concept of the dynamic unconscious and on psychoanalytic theory of personality development, including Hartmann's theories of adaptation and Erikson's concepts of life stages. Psychotropic drugs have decreased suffering and increased function in psychiatric patients, but they have by no means solved all problems related to understanding and treating psychiatric illness.

Psychoanalysis as a method of treatment has always been the treatment of choice in a small percentage of all patients—i.e., certain neuroses and character disorders—and for these patients it continues to be the most definitive etiologic therapy we have. Knowledge gained from clinical psychoanalysis and related research, including research into human development, continues to increase our understanding and our therapeutic efficacy.

What is generally the best approach to take in referring a patient to a psychiatrist?

Patients needing referral to a psychiatrist are not much different than patients needing referral to other specialists. They are usually aware of subjective discomfort—i.e., anxiety, depression, or other symptoms, and can be sent for help to a physician who specializes in treating these kinds of problems. A matter-of-fact referral can be quite useful and reassuring to the patient as can an expression of the referring doctor's continuing interest in the patient and the results of the referral.

Patients who do not have subjective symptoms—i.e., psychopaths, delinquents, some marriage problems—are much more difficult to refer successfully. These are patients about whom others complain, who themselves may feel little but social distress. Pressuring such patients to see a psychiatrist may not be possible until such time as the problems get bad enough that the patient himself is suffering.

How should you suggest a physician manage a depressed adolescent school dropout?

Depression in adolescence should be
Continued on page 12

Next In Consultation

DR. SPENCER K. KOERNER, Chief, Division of Pulmonary Medicine, Montefiore Hospital and Medical Center, New York.

. . . will discuss the development of respiratory intensive care units and what they have achieved and answer such questions as:

- What pulmonary function tests can the physician do in his office? When should he turn to the laboratory?
- What kind of home regimen helps the patient with chronic obstructive lung disease?
- What are the prospects for lung transplants?

Dressing Bag Eases Postop Management of Amputation Area

Medical Tribune World Service

VIENNA—A "dressing bag" that permits the surgeon to influence blood flow, degree of edema, and temperature of the amputation stump postoperatively, as well as ensuring sterility and reducing humidity, has been developed by the biomechanical research and development unit of the Department of Health and Social Security, London.

The surgeon is also enabled to inspect the operative site at all times without disturbing the control of the environment, Dr. Robert G. Redhead told the first International Congress on Prosthetics Techniques and Functional Rehabilitation here.

The bag has been used after six below-knee amputations and six cases of hand surgery, Dr. Redhead reported. He said that, while the numbers are not yet large enough for statistical comparisons, the results so far have been encouraging. In theory, the bag would also be useful for the treatment of burns of the extremities.

The "dressing bag" maintains a sterile environment for postoperative stump management and permits the surgeon to influence blood flow, degree of edema, and temperature.

Management of Area Crucial

"The management of the stump environment during the postoperative period has a profound effect on the chances of achieving successful healing," Dr. Redhead declared.

Drawbacks of conventional methods of stump management led to the development of the dressing bag, he said. Although excellent results have been obtained with plaster casts applied immediately postoperatively, the application of such casts requires a great deal of skill and, once applied, they are difficult to change, he noted. In addition, such casts provide only partial protection from bacterial contamination and provide no control over temperature and humidity.

With the new system, the stump environment is controlled by means of air flow. The dressing bag is connected to a control console on one end and is attached to the stump by a pleated seal similar to those used for the skirts of hovercraft. This seal allows the escape of air but not its entry, since the pressure inside the bag is higher than the outside pressure.

"The seal itself exerts no pressure on the limb greater than the pressure within the dressing bag and therefore cannot have any tourniquet effect," Dr. Redhead noted.

In addition, the apparatus controls edema and yet permits blood flow to the limb by alternation between a high- and a low-pressure phase.

"During the high-pressure part of the pressure cycle in the dressing bag, blood is squeezed through the capillaries and veins in the stump and, at a slower rate, there is a reduction in the volume of any edema present," the physician said. "During the low-pressure part of the pressure cycle, the vascular bed refills more rapidly than the edema volume is restored. The next high-pressure phase of the pressure cycle is therefore timed to start just after the vascular bed is refilled but before the edema volume is restored."

Edema Volume Declines

If this pressure cycle is repeated many times, there will be gradual diminution of edema volume, while the blood volume is maintained, Dr. Redhead declared. The duration of the high-pressure/low-pressure cycles is set according to the time taken for the skin to blanch and blush, respectively.

There is at present no specific humidity control in the dressing bag, but the relative humidity of the air in the bag is reduced in comparison with external air because it has been heated. To ensure sterility within the bag, the air is first passed through a bacterial filter.

While the patient cannot walk during this treatment, he is able to carry out a normal program of postoperative exercises, Dr. Redhead said.

Simple Screening Test Is Reported to Detect Riboflavin Deficiency

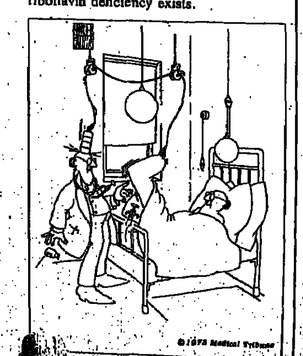
Medical Tribune Report

ATLANTIC CITY, N.J.—Development of a simple screening test for riboflavin deficiency was reported here by three New York Medical College investigators to the Federation of American Societies for Experimental Biology.

Drs. Harold S. Cole, Rafael Lopez, and Jack M. Cooperman, of the Department of Pediatrics, said that the test—a modification of the Glatzle method, which requires highly specialized facilities—can be performed routinely by an ordinary medical laboratory.

The new technique is based on the fact that erythrocyte glutathione reductase (EGR) is, in the normal state, saturated with flavin adenine dinucleotide (FAD) and that the activity of EGR is a measure of the extent of this saturation.

To perform the test, a technician takes a blood sample from the patient and gauges the level of activity of EGR. The technician then adds FAD to the sample, and if the addition causes an increase of more than 20 per cent in EGR activity, a riboflavin deficiency exists.



3,400 Screened, 5 Colorectal Cancers Found

Medical Tribune Report

PRINCETON, N.J.—At least five cases of colon-rectum cancer were detected in a mass screening of 3,400 persons in Mercer County, N.J., Dr. James Hastings of Princeton reported here.

Dr. Hastings, who headed the screening, said that, in addition to the cancers, 10 per cent of those examined had disorders requiring medical attention, including diverticulitis, hemorrhoids, and prostatic disease.

According to American Cancer Society projections, colon-rectum cancer this year will strike 79,000 Americans and kill 47,000.

A total of 2,933 persons availed themselves of a digital rectal examination offered by the screening teams. All visitors received three "Hemoccult" slides and dietary instructions to take home. Completed slides were mailed to the American Cancer Society.

Uses Thin Stool Specimen

To use the guiac-impregnated slide, the subject smears a very thin stool specimen on the surface. In his office, the physician applies a developer, and the emergence of any trace of blue indicates the presence of occult blood. Slide processing takes about 30 seconds.

Dr. Hastings reported that, of 2,642 test slides that were returned, examination disclosed positive findings in 159. Follow-up studies in 52 subjects uncovered the five asymptomatic bowel cancers as well as other disorders, such as diverticulitis and polyps. Thirty of the 52 were false-positives, a rate attributed by Dr. Hastings to the failure of subjects to follow the prescribed meat-free, high-roughage diet. The slides employed in the screening program are marketed by Smith-Kline Diagnostics, a division of Smith Kline & French Laboratories.

Lower Birth Rate Leads Hospitals To New Approaches to Ob Facilities

Medical Tribune Report

CHICAGO—A survey by the American Hospital Association has disclosed that many hospitals have started converting, pooling, or trading off their obstetric facilities as a result of the nation's declining birth rate. By converting some of these facilities to other uses, they are saving millions of dollars in new construction costs, the association said.

Recent A.H.A. statistics show that between 1968 and 1972 there was a 6.1 per cent decrease in hospital births, from 3,119,639 to 2,927,864, and a drop in average length of stay for obstetric patients from 4.35 days to 4.14 days. The occupancy rate of newborn beds declined from 40 per cent in 1968 to 38 per cent in 1972.

Through an annual survey taken of all hospitals, the A.H.A. noted a 6 per cent drop in hospitals reporting births over the past 10 years, a figure that could indicate a comparable decline in hospitals offering obstetric services.

"The dramatic changes in birth rates are causing hospitals to shift gears and close down units when they are being underutilized," said John Alexander McMahon, A.H.A. president. "By converting obstetrical beds to use by other growing services, hospitals have been able to increase efficiency, quality of care, and avoid spending money for new construction."

Earlier Limb-Fitting Urged

VANCOUVER, B.C.—A Polish surgeon said here that fitting artificial limbs on the operating table immediately after amputation gives more rehabilitation success than traditional methods of waiting weeks or months before fitting the limb.

Dr. Marian Weiss, director of the Institute of Rehabilitation and Reconstructive Surgery, Warsaw Academy of Medicine, made the recommendation at an International Symposium on Rehabilitation of the Industrially Disabled.

He based it on experience with patients who underwent amputation at his academy from 1960 to 1972.

Dr. Weiss, who is a rehabilitation adviser to the World Health Organization, said that instant fitting of the artificial limbs has these advantages: faster walking and a fitness level that equals within eight weeks that obtained after one year with conventional techniques; greater physical strength and endurance; better sleep and lessened neurotic reactions or states of fear; less shrinkage of thigh stumps; and full disappearance of "phantom feelings" within four weeks, as opposed to at least a year with traditional methods.

Spinal Centers Needed

VANCOUVER, B.C.—Special centers should be set up to treat spinal injuries, an International Symposium on Rehabilitation of the Industrially Disabled was told here.

Kenneth Jenkins, president of the Australian Council for Rehabilitation of the Disabled and chairman of the World Commission on Vocational Rehabilitation, said the proposal resulted from recommendations of the symposium's workshop on spinal problems.

He said that more than 25 per cent of spinal cord cases are associated with injuries and need special treatment.

"Acute care hospital treatment is far too long, far too costly, and deprives patients of their earning power while they are hospitalized," he said.

Treating Shock Patients

DUBLIN—Dr. Björn Ibsen, of Kommunshospitalet, Copenhagen, said that if a patient in shock is treated in an air-conditioned room, where temperature can be maintained constant, treatment can be guided by measuring rectal temperature and peripheral skin temperature on the thumbs and big toes.

Changes in the body temperatures will be due to alteration in the patient's hemodynamics caused by either the disease or the treatment, he told a meeting of the Royal College of Surgeons, Ireland.

Foil Drains Glaucoma

PRAGUE—A Hydron capillary foil, 3-5 mm. wide, used in severe, painful cases of glaucoma to form a permanent drainage provokes none of the unfavorable reactions that occur when other plastic materials are employed, according to the experience of Czechoslovak eye surgeons.

The hydrophilous gel, a polymerized monomer mixture of hydroxylethyl methacrylate and glycerin, developed at the Institute for Macromolecular Chemistry here, is normally used for contact lenses.

Parallel polyamide fibers wound around a glass plate are placed into the monomer mixture, which turns into a hydrogel by polymerization. After the process has been completed, the fibers are dissolved and washed out with sulfuric acid, leaving in the gel foil a system of regularly spaced free capillaries with smooth walls.

In the surgical treatment of glaucoma the capillary system permits microdrainage and even escape of particles up to 0.1 mm. in diameter that may have entered the anterior chamber during or after operation.

The foil will take a load of up to 1,000 Gm. without closure of the lumina.

Arteriography Aids Decision On Surgery for Renal Tumor

Medical Tribune Report

WASHINGTON—Arteriographic evaluation to determine the advisability of surgery for renal neoplasms was urged at the National Conference on Urologic Cancer here by Dr. Erich K. Lang, Professor of Radiology and head of the department at Louisiana State University School of Medicine at Shreveport.

DR. LANG

An "excellent" correlation with assessments gained from surgical exploration was achieved by this means in 120 patients with renal cell carcinoma, he reported. Further, survival statistics in 146 patients staged arteriographically paralleled those for patients staged by means of surgical exploration and histopathologic study.

In contrast to most other roentgenographic diagnostic techniques—which allow for diagnosis only on the basis of secondary tumor effect—renal arteriography affords "direct demonstration and visualization of the tumor itself," Dr. Lang said, adding that decision making in regard to management can therefore be carried out on the basis of precise information.

"The ability of the arteriogram to demonstrate the primary tumor, extension of the primary tumor into adjacent structures, and metastatic tumor," he said, "makes this modality most useful for preoperative assessment and staging of renal neoplasms."

Staging by arteriography relies on visualization of abnormal arterial patterns in the organ of origin, adjacent organs, or distant organs, he noted.

Characteristically, the arteriographic picture of a hypernephroma is a network of irregular vessels of variable caliber, aneurysms, and arteriovenous shunts, Dr. Lang said. The vessel irregularity is "particularly well seen in the perimeter of expanding lesions."

In stage 1, he continued, neoplasms derive all of their vascular supply from renal vessels. Intrarenal vessels supply stage 1A lesions, and capsular arteries contribute to stage 1B lesions. Stage 2 neoplasms extend outside the confines of the renal vessel. At stage 2A, however, the lesion is contiguous with the primary lesion in the kidney. Stage 2B lesions invade renal vein, and stage 2C lesions invade regional lymph nodes. If tumor vessels are identified in distant organs, the disease is designated stage 3. Stage 3A denotes tumor extension into the inferior vena cava; stage 3B, metastases to periaortic nodes; and stage 3C, metastasis to distant organs.

Based on such arteriographic assessment, 109 of 146 patients with renal neoplasms were proposed as candidates for nephrectomy or radical nephrectomy with node dissection. Of the 109 patients, 90 proved to have resectable lesions.

"The sharp decline in five-year survivors harboring hypernephromas staged arteriographically as 2B or more advanced lesions again parallels survival statistics of similar surgically staged patients and affirms failure of present treatment modalities to control such advanced disease," Dr. Lang said.

Device Overcomes Arm Paralysis in Use of Phone

A device enabling patients with paralysis of the arms to receive and dial their own telephone calls has been developed by Dr. Olle Hook, of the University of Göteborg, and Bengt Lindberg, Ph.D., Chalmers Institute of Technology. The operating unit consists of two microswitches that can be operated by slight pressure from a hand, foot, or chin or by sucking or puffing.

Diet for PKU Ended Safely at Age Five

Medical Tribune Report

SAN FRANCISCO—The majority of patients with phenylketonuria can be safely taken off a low phenylalanine diet at the age of five, Dr. William B. Hanley, of the University of Toronto, told the Society for Pediatric Research here.

He said that 61 PKU patients who have been off their diets for one to five or more years show few changes in I.Q., behavior, or electroencephalograms.

No I.Q. changes were noted in 49 of the patients, while five had a drop of more than 10 points and seven showed an increase of up to 23 points.

No behavioral changes were seen in 52 of the group, while five improved and four deteriorated, Dr. Hanley said.

None of the patients have had seizures, and 49 follow-up electroencephalograms showed no change in 43, a slight change in four, and definite abnormal patterns in two.

Hair and skin changes were assessed in 52 patients. Nine developed and retained lighter hair color, and none developed skin rashes.

While a majority of patients can safely be taken off the diet at five, long-term follow-up is needed so that the diet can be reinstituted if necessary, Dr. Hanley said.

Dr. Lydia Linsao was coauthor of the presentation.

Three Receive Citation From Family Physicians

NEW YORK—The Certificate of Commendation of the American Academy of Family Physicians, a special award for communications professionals, was presented here to Paul Cunningham, interviewer on the NBC "Today" show; David Hendin, science editor of Newspaper Enterprise Association, and Donald Fouser, originator and director of "VD Blues," the Public Broadcasting System special.

Cyclophosphamide Cystitis 'Can Be Fatal'

Medical Tribune Report

NEW YORK—Cyclophosphamide therapy can produce varying degrees of hemorrhagic cystitis, a Harvard investigator warned here and proposed measures to avoid this potentially fatal complication.

Dr. Alan H. Bennett detailed three cases and their management and pointed out that "with the increasing use of cyclophosphamide in various malignancies and hematological disorders, as well as the newer application in renal disease, especially in children, many more cases of hemorrhagic cystitis can be anticipated."

The occurrence of cystitis is usually dose-related and can occur whether the agent is given orally or intravenously after 20 weeks or more of therapy, he told the 68th annual meeting of the American Urological Association. He noted that the incidence of cystitis is higher after intravenous cyclophosphamide therapy.

The treatment of cyclophosphamide cystitis, said Dr. Bennett, depends upon the severity of the problem. Cystoscopy is indicated in all patients with hematuria. Any obvious bleeding points should be fulgurated. In many cases, he noted, the hematuria appears to be self-limiting and will stop with the cessation of cyclophosphamide therapy.

Conservative treatment is encouraged, he declared, and this includes bed rest and high fluid intake. The short-term use of prednisone in large doses may reduce edema and the inflammatory reaction seen in acute cases.

Hematuria May Threaten Life

Occasionally, he said, hematuria is unremitting and threatens the life of a patient. Suprapubic cystotomy and open fulguration with placement of a suprapubic tube for continuous irrigation may be helpful, "but it might become necessary to perform cystectomy with urinary diversion as a lifesaving measure."

Dr. Bennett warned that the patient on cyclophosphamide should be managed very carefully to decrease the incidence and severity of hemorrhagic cystitis. When possible, the drug should be used orally and in doses not exceeding 100 mg./day in adults or 2.5 mg./Kg. in children.

A high fluid intake must be maintained and patients should be instructed to drink fluids at night so that a high urinary output can be maintained for 24 hours a day. Routine urinalysis should be performed every month while the patient is on the treatment and for up to one year after cessation of therapy, he said.

He warned that cyclophosphamide should not be given to patients with a prior history of bladder difficulties. The drug should be stopped immediately if any lower urinary tract symptoms occur or if microscopic or gross hematuria begins.

"In patients who have developed hemorrhagic cystitis," he emphasized, "treatment with cyclophosphamide should not be reinstituted even if cystoscopic examination may return to normal. Routine periodic cystoscopy might help to avoid serious complication as subtle changes in the bladder might be recognized before hemorrhagic cystitis begins."

Stress Affects Goiter

Medical Tribune World Service

EIN KAREM, JERUSALEM—Family stress situations are a significant factor in precipitation of overactive goiter, according to physicians at Hadassah-Hebrew University Medical Center here. Drs. Ernest N. Ehrenfeld and M. Levy reported three cases of thyrotoxicosis in one family following a period of severe stress.

Lymphosarcoma Therapy

ATLANTIC CITY, N.J.—Intensive combination chemotherapy in the treatment of lymphosarcoma does not appear to improve the response rate over that of chemotherapy with a single induction agent and single alkylating agent for maintenance, and it may even increase the toxicity.

This was the experience a group of clinicians from Roswell Park Memorial Institute, Buffalo, N.Y., reported to the 64th annual meeting of the American Association for Cancer Research.

Drs. Jerome H. Kaufman, William Aungst, and Leon Stutzman, of Roswell Park, and Dr. Ediz Ezdinli, of the Mount Sinai Hospital Medical Center, Chicago, found that intensive combination chemotherapy for six months resulted in a partial response in 91 per cent of patients and a complete response in 77 per cent, while short-term chemotherapy with a single induction agent and single alkylating agent for maintenance resulted in a partial response in 88 per cent and a complete response in 75 per cent of patients.

Survival from onset of therapy was 58 per cent in the first group and 66 per cent in the second group.

The study was conducted among 63 patients with stage 3 and 4 lymphocytic-type lymphoma, with a median observation of 22 months.

Patients' Rights Urged

SOESTERBERG, THE NETHERLANDS—The right of a patient to information on his treatment and prescribed medicines should be given the force of law, a professor of health law told a congress of pharmacologic students here.

The stand by Dr. J. F. Rang, of Leiden *University*, is contrary to the position of the National Medical Disciplinary Board (Centraal Medisch Tuchtcollege), which holds that to divulge such information is in the discretion of the individual physician.

Dr. Rang, addressing the General Netherlands Pharmaceutical Students Society, said that "the opposite should be the rule, unless giving information clearly is not in the interest of the patient."

Canada Bans Marking Dye

OTTAWA—Canada has temporarily banned the food color benzyl violet 4B, the dye used to mark government grades on meats and to color pet foods, until the manufacturer can prove the dye is safe for human use.

Federal officials with the health protection branch said that recent toxicologic data suggest the dye could cause adverse effects when consumed at high levels by rats.

Food processors have been given until August 1 to reformulate products containing the dye (the same as violet no. 1, recently suspended in the United States).

Road Rules on Drugs Asked

HELSINKI—Steps are being taken by Finland's Traffic Ministry to reduce the possible danger of prescription medicines to road safety. A special committee has been set up to develop regulations.

The committee chairman, Dr. Juhana Idanpann-Heikkila, chief pharmacologist at the National Board of Health, said that one or two of every five patients in psychiatric outpatient clinics take heavy central nervous system medication and still drive their automobiles.

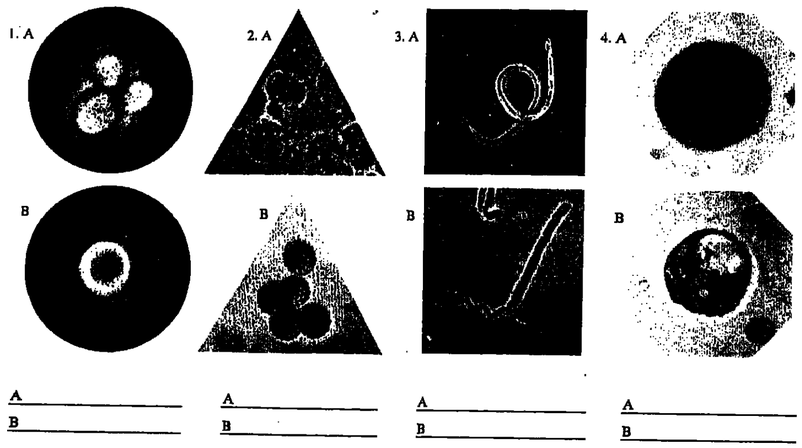
Many of Finland's drunken drivers have been found to have used both alcohol and drugs, he said.

Families' Capsules Tallied

TEL AVIV, ISRAEL—The average family in this country has 550 capsules of various kinds in the medicine cabinet, according to a recent survey here.

Puzzling Pairs

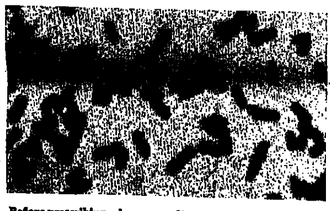
Can you identify these look-alike findings in urinary sediment? Spaces are provided below for your answers. One of a series of quizzes based on Roche's handbook, "Urine Under the Microscope."



A_____ A_____ A_____ A_____
B_____ B_____ B_____ B_____

For correct answers and identifying clues, see bottom of page.

No Puzzle Here



E. coli showing typical gram-negative rods. The coliforms—particularly *Escherichia coli*—are the primary pathogens in approximately 90 per cent of initial urinary tract infections.*

*Beeson, P. B.: "Enteric Bacterial Infections," in Beeson, P. B., and McDermott, W. (eds.): *Cecil-Loeb Textbook of Medicine*, ed. 12, Philadelphia, W. B. Saunders Co., 1967, vol. 1, p. 230.

For prompt antibacterial levels in blood and urine: Effective antibacterial levels of Gantanol in both blood and urine are established in from 2 to 3 hours after initial 2-Gm adult dose.

When susceptible urinary bacterial invaders are identified in nonobstructed cystitis and pyelonephritis, Gantanol (sulfamethoxazole) is a logical choice. It controls susceptible *E. coli*, the most common pathogen in acute urinary tract infections, and is also highly effective against other susceptible bacteria most often implicated: *Klebsiella-Aerobacter, Staph. aureus* and *Proteus mirabilis*.

For around-the-clock coverage: Each subsequent 1-Gm dose offers up to 12 hours of antibacterial activity. This is especially important during the night, when urinary retention favors bacterial proliferation. A *t.i.d.* dosage schedule is recommended for more severe infections.

For efficacy in nonobstructed acute, chronic and recurrent cystitis and pyelonephritis, when due to susceptible organisms: Gantanol Tablets or pleasant-tasting Suspension can provide your patients with the dependable antibacterial action they need. However, the usual precautions in sulfonamide therapy should be observed, including maintenance of adequate fluid intake, frequent c.b.c.'s and urinalyses with microscopic examination. Common side effects include nausea, vomiting and diarrhea. (It should also be noted that the increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents including sulfonamides, especially in chronic or recurrent u.t.i.)

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. *Note:* Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).
Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.
Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

Correct answers to "Puzzling Pairs" quiz.

1. (A) *Candida albicans.* Note budding and variation in size of daughter spores.
   (B) RBC. Note central portion representing characteristic concavity of RBC.
2. (A) Polymorphonuclear leucocytes. Note partially obscured lobulated nucleus and irregular granules.
   (B) Ragweed. Note geometric knobby protrusions of the ragweed particle.
3. (A) *Necator americanus* (larval form). Note distinctive head and details of internal organs.
   (B) Convoluted cast. Note diffuse fine granular appearance throughout and corkscrew shape of terminal portion.
4. (A) *Entamoeba histolytica.* Note chromatoidal bodies.
   (B) Histiocyte. Note phagocytic vacuoles.

In nonobstructed cystitis due to susceptible organisms

Gantanol® (sulfamethoxazole) B.I.D.

Basic Therapy

ROCHE Roche Laboratories Division of Hoffmann-La Roche Inc. Nutley, N.J. 07110

The Only Independent Medical Newspaper in the U.S.

Medical Tribune

and Medical News
Published by Medical Tribune, Inc.

Advisory Board
JOHN ADRIANI, M.D. • JULES H. MASSERMAN, M.D. • ROBERT A. CHASE, M.D.
ARTHUR M. MASTER, M.D. • RENE J. DUBOS, PH.D. • ALTON OCHSNER, M.D.
BERNARD LOWN, M.D. • LEO G. RIGLER, M.D. • ALBERT B. SABIN, M.D.

ARTHUR M. SACKLER, M.D.
International Publisher

WILLIAM F. B. O'DONNELL, *General Manager* — RICHARD S. GUBNER, M.D., *Associate Editor*
NATHAN HORWITZ, *News Editor* — WILLIAM PRIFTIS, *Layout Editor*

880 Third Avenue, New York, N.Y., 10022 • Telephone: 421-4000
ABC *Circulation audited by Business Publications Audit of Circulation, Inc.*

For a Free Scientific Press

Continued from page 1

on Linus Pauling and on a group of diabetologists who disagreed with a controversial government-sponsored study. It was at that time we were particularly moved by a plea for the freedom of speech made by Sen. Sam J. Ervin: *"While I hate their ideas . . . [I] fight for their right to think the thoughts and speak the words I hate. If we ever reach the condition in this country that we attempt to have free speech for everybody except those whose ideas we hate, not only free speech but freedom itself are out in our society."*

Senator Ervin's observations were fundamental American philosophy but equally pertinent to science. In several editorials, at the end of 1971, we made reference to Senator Ervin's comments on the First Amendment and commented that his Senate Committee on Constitutional Rights is doing yeoman's work. One MEDICAL TRIBUNE editorial went on, *"It has been said that the price of freedom is eternal vigilance, and we are fortunate indeed to have Senator Ervin exercising this vigilance."* The headlines of today underline the validity of that observation. You may enjoy the rest of the editorial, which we filed but did not publish then. Perhaps it is even more appropriate today:

On the Level of Medical Debate

IT WOULD SEEM that recent differences of opinion in medicine are associated with a declining level in the character of debate. The amenities and courtesies which have been customary seem to have been swept aside by an egalitarian tide of "blunt" behavior and disregard for the achievements or points of view of others. It is not all to the good.

In an issue of MEDICAL TRIBUNE, in a "Current Opinion" on acupuncture, there was a gratuitous insert which attacked "a prominent scientist in an unrelated field [who] on dubious evidence extols the virtues of vitamin C for the common cold and gains many followers."

The Medical Press Must Be Free

MEDICAL TRIBUNE, in its conviction that the medical press must be free, published this in its columns despite our belief that the author had neither justification to insert the comment nor to juxtapose that statement against the observation that "this is an era of health faddism, mysticism, disaffection with the medical establishment, and disenchantment with Western ideas. . . . Exotic doctrines such as Zen Buddhism and a variety of cults . . . represent an anti-intellectual and antiscientific trend."

The author of that "Current Opinion" rightly attacked the presently popular "anti-intellectual" and "antiscientific" trend but depreciated the validity of the critical point he was making by coupling his own comments with pejorative comments about a great scientist with whom he disagreed. He failed to see the fundamental thrust of the man who advocated high vitamin dosage; that is, that the heterogeneity of man and experimental data suggest that an individual or different organs may have a differential of 20- to 100-fold in requirements for essential metabolic substances.

A Prodigious Mind

To term Linus Pauling "a prominent scientist in an unrelated field," as that physician did, is probably the understatement of our decade as the characterization of the man who was twice named Nobel Laureate and whose work constitutes one of the foundations for molecular biology, molecular genetics, and ultimately molecular medicine. In *The Double Helix*, in which J. D. Watson tells the story of the discovery of the structure of DNA, Linus Pauling is described as "the greatest of all chemists," "a giant" with "a prodigious mind."

The Deterioration of Debate

At an even lower level one noted, in the *Annals of Internal Medicine* (*75:303-306, 1971*), an attack by one physician on colleagues which was both personal and unrelated to the subject at issue. To interject reference to the Nuremberg trials in a medical commentary on scientific controversy over the continuing use in a proper medical setting of a widely used and accepted therapeutic agent is a horrifying lack of recognition of what happened in Germany and what the Nuremberg trials were all about. And to write, *"Dr. Diabetes has a long-haired son who smokes 'pot' and an unmarried daughter who takes the 'pill.' The last thing he wanted to hear in St. Louis was that a medication he has been giving his patients for 13 years might be doing them in"* is to further compound the deterioration of debate.

It is not excused by the author's subsequent statement, *"It seems to me terribly important that public attacks on personal integrity not become a tolerable dimension in medical disputes."* If he believed that, then he should not have published what appears to be vilification of his colleagues.

In this situation both MEDICAL TRIBUNE and the *Annals of Internal Medicine* published material which really should not have been submitted in the first place. In other situations it has come to our attention that scientific publications have refused material which does *"not fit in with their philosophies."* We know of no philosophy other than responsible reporting of the truth, of data, of facts, of research.

The responsibility Of a free scientific press

We feel strongly that the medical press should be available to all, including those with whose views we take issue. The responsibility of a free scientific press is to make available its pages for the opinions of all and the obligation of those who use this freedom is that they, in turn, be responsible.

A.M.S.

"Gladys, who recommended this doctor?"

LETTERS TO TRIBUNE

Thought for Food...

Editor, MEDICAL TRIBUNE:

Your editorial and the guest editorial by Dr. Shanklin (MEDICAL TRIBUNE, May 23) are most appropriate.

As you point out, nutrition is not the only factor involved in a healthy pregnancy. Nor has the exact significance of the various food elements been clearly delineated. However, the importance of applying the information that is already known about nutrition and other aspects of pregnancy cannot be overemphasized.

Quality of life in the United States could be enhanced more by the use of already acquired knowledge in the case of mothers and infants than by any other measure. Now is the time to recognize this.

MICHAEL NEWTON, M.D., FACOG
American College of Obstetricians and Gynecologists
Chicago, Ill.

■

And Food for Thought

Editor, MEDICAL TRIBUNE:

Your editorial on "Pregnancy Is Nutritional Stress" and Dr. Douglas R. Shanklin's guest editorial calling for "a truly physiological approach to pregnancy, especially with regard to nutrition," both are certainly timely and laudable.

Your editorial also calls for a humane approach, which is equally laudable, but requires not only scientific management of pregnancies but also an inquiry as to whether or not the pregnancy is wanted at all.

Women who do not want to be pregnant often are not motivated to adhere to appropriate nutrition for themselves and the fetus, even if available and prescribed, any more than they are prepared to nurture their children adequately after birth.

A truly scientific and humane approach, therefore, would take not only the nutritional factors into account but also the question of whether, for the sake of the mother's health and welfare, this pregnancy should be allowed to go to term at all.

STEPHEN FLECK, M.D.
Yale University School of Medicine
New Haven, Conn.

■

Preparental Education

Editor, MEDICAL TRIBUNE:

You have given a tremendous impetus to a point of view I have held for many years in reporting Dr. Sackler's interview with Dr. Heinz E. Lehmann, of McGill University (MEDICAL TRIBUNE, May 2, 9, and 16).

Efforts need to be continued in this area to convince society of the inestimable value to future generations if we would begin now to teach young people (in their teens) how to become "good" parents.

LEONARD H. BISKIND, M.D.
Cleveland Heights, Ohio

■

Vaccination at Issue

Editor, MEDICAL TRIBUNE:

If a mere practicing pediatrician may take issue with a Visiting Professor of Epidemiology at Harvard Medical School, I should like to do just that.

In MEDICAL TRIBUNE of May 16, Dr. Alexander D. Langmuir recommended that all hospitals should have routine smallpox vaccinations for personnel. This, I feel, is a very controversial statement.

As in all things medical, we as physicians must weigh the risk versus reward in smallpox vaccinations. If, as the U.S. Public Health Service says, routine smallpox vaccination should not be given in this country, then it should be stopped. Period.

We are raising a generation of children now who have not had smallpox vaccination. They will be entering children's hospitals and pediatric wards with many illnesses, such as immune deficiencies, eczema, etc. The presence of a hospital attendant who has had recent smallpox vaccination can pose an extreme threat to these children.

Also, as our pediatric patients grow up, many of them will go to work in hospitals. If the hospitals are going to require that the 16-year-old candystriper or the 18-year-old student nurse be vaccinated, I would rather do it now, while they are one or two years old, than have them hit with a primary vaccinia reaction at an age when they can ill afford the time loss and where their susceptibility to encephalitic complications may well be greater. Let's either vaccinate or not vaccinate!

I particularly object to the statement by Dr. Langmuir that the hospital would incur "unquestioned liability" if an episode of smallpox should occur. This is an unjustified and reckless statement. There is too great a tendency nowadays for a person who is pushing a particular proposal to say that somebody is going to be sued if that proposal is not accepted and adhered to by everybody.

There is plenty of room for debate as to whether or not hospitals should require smallpox vaccination, in view of the extremely small possibility of a case of smallpox being introduced into this country. I might say that a hospital now requiring smallpox vaccination might be liable for any complications that occurred. I might say it, but I won't, because I do not think that the liability issue should be dragged into this by me, by Dr. Langmuir, or by anybody else.

FORREST P. WHITE, M.D.
Norfolk, Va.

Bronx Team Identifies Algae As Cause of Tropical Sprue

Continued from page 1

An unusual aspect of the studies, Dr. Bernstein told the meeting of the American Gastroenterological Association, is that a healthy physician volunteered to ingest the suspected algae and to submit to a series of intestinal biopsies in order to test the team's hypothesis.

The research group's initial speculations about a pathogenic algal organism, Dr. Bernstein noted, were spurred by the knowledge that tropical sprue has a seasonal incidence, infectious properties, and lack of person-to-person transmission and that it is geographically restricted. The fact that thorough study by other investigators had failed to uncover a pathogen, the physician said, suggested that "the disease must be caused by something that no one had thought of."

His attention, he continued, was drawn to the possibility of an algal pathogen by a 40-year-old report from Dr. Bailey K. Ashford, "the father of sprue research in this hemisphere," who noted that he had cultured chlorophyl-less algae from the stool of two patients with sprue in San Juan, Puerto Rico. Although Dr. Ashford did not believe the organism was causally related to the syndrome, specimens were kept alive in the Algal Culture Center at Indiana University.

In a follow-up on Ashford's hint, the Bronx team found that when algae were fed to animals, the organisms could be cultured from the stool, but only while the animals were fed the algae, suggesting that Dr. Ashford's patients had been ingesting algae at the time their stools were cultured.

Drs. Bernstein and Lepow then restudied the intestinal biopsies of some 24 of their sprue patients, and although they did not find algal organisms, "at magnifications of about 1,000 [we] began to notice PAS positive bodies, usually paired, in cells of the crypts.... Numerous paired bodies could be seen in both the lamina propria and the epithelial cells of the villi of 24 out of 24 sprue biopsies."

The paired bodies also showed up in agar plates that were streaked with the algae and serum of sprue patients, Dr. Bernstein said.

Algae Suspended in Serum

"Remembering one line in the Ashford article which stated, 'Occasionally a motile body is seen within the algal cell,' we suspended the algae in warm serum on a warm microscope slide," the investigator went on. Within 20 minutes, granules inside the cell bodies became active and motile, suggesting that they were algal gametes. When these were introduced into tissue culture composed of epithelial cells isolated from rat liver, the cells lysed within 24 to 48 hours and "such cells stained with PAS showed innumerable paired organisms within the cytoplasm, which we feel represent the zygote phase of the alga."

In the culminating phase of the research, "an informed, consenting physician," having studied all of the data, underwent a series of base-line studies and "began the ingestion of 6 billion Prototheca cells per day in tap water," Dr. Bernstein reported.

"He remained asymptomatic until day 16, when he developed malaise, ileus, fever, nausea and vomiting, which remitted after four hours. Biopsies, taken 96 hours after the acute episode, demonstrated loss of villous height, blunting, and infiltration of the lamina propria. Silver stains of the normal and pathologic biopsies showed the infiltration of epithelial cells in the abnormal biopsy, with silver positive diploid bodies identical with those observed in tissue culture, agar, and in the biopsies of patients with tropical sprue."

In summary, said Dr. Bernstein, "A colorless alga, Prototheca portoricensis, found in the stools of patients with tropical sprue 40 years ago...was shown to possess previously unknown motile bodies, released by contact with mammalian serum." The zygote resulting from the conjugation of these gametes reproduces in epithelial cell tissue culture, is cytopathic, can cause cell death within 48 hours, and is "identical with forms found in the intestinal biopsies of patients with tropical sprue."

Quokka Makes Debut in Cincinnati Lab

A Rottnest quokka is a wallaby, or small edition of the kangaroo, found only on Rottnest Island near Perth in Western Australia. Five of the small animals were recently brought to the University of Cincinnati by Dr. Shirley H. Bryant to aid in his study of myotonia. The muscular disorder, similar to the human disease, is developed by the quokkas, particularly in captivity, where they may not receive a proper diet.

Careful Neurologic Study Urged in Scoliosis

Medical Tribune Report

BOSTON—Every patient with scoliosis requires careful neurologic evaluation, the annual meeting of the American Academy of Neurology was cautioned here.

Although many neuromuscular disorders frequently accompany scoliosis, patients with this disorder are not usually seen by neurologists unless some obvious neurologic dysfunction is evident, Dr. David A. Rothner said.

Because he and a colleague, Dr. Abe M. Chutorian, suspected that such additional disorders may indeed be present but escape detection, they performed neurologic evaluation of 100 children as they presented at Columbia-Presbyterian Medical Center, New York, with the general complaint of scoliosis.

Certain Children Excluded

Children designated or suspected beforehand as having a neuromuscular disorder in addition to their scoliosis were excluded from this study.

Of the 100, 66 were hospital patients and 34 were outpatients. Each was given a thorough physical examination, x-rays were taken, and a detailed neurodiagnostic work-up was performed.

Seventy-two of the children were found to have typical idiopathic scoliosis. Forty-one per cent of this group had a family history of the disorder.

In the idiopathic group, no additional neuromuscular problems were discovered. Forty-seven of the youngsters had surgical correction with no complications, and the remainder were either followed without specific therapy or else fitted with a Milwaukee brace.

Nine children were found with congenital scoliosis, as defined by the presence of a congenital anomaly of the bony spine.

Three of the nine had a family history of scoliosis; two were mentally retarded; two had diastematomyelia; one had a single kidney; and one had coexisting neurofibromatosis.

Seven of the 100 patients were categorized as having neuromuscular scoliosis. Of this group, two were diagnosed as having diastematomyelia, two had familial myopathy, one had hydromyelia, another had chronic polyneuropathy, and one was found to have Charcot-Marie-Tooth disease.

In recommending careful neurologic evaluation of all patients with scoliosis, Dr. Rothner said:

"It is important to identify associated disorders early so that genetic counseling can be offered when indicated and to identify those youngsters in whom the neurological impairment will progress. The evaluations are also necessary so that appropriate therapy can be planned and so possible complications to surgery can be identified."

Added Evidence Shows Bacteria May Cause Multiple Sclerosis

From Boston

► Additional evidence that a slow-acting bacteria or virus may be a cause of multiple sclerosis was outlined by Dr. Richard Eastman of Boston, who found 14 cases of the disease in one Massachusetts town of 10,000 population—two to three times the rate for the northeastern United States.

Searching for a common factor among these patients, he found that eight of them had lived in the community during a series of sewage contamination episodes that occurred between 1932 and 1936.

The eight had been born in the community or had lived there since childhood. In 1934, midway through the contamination episodes, they were of a mean age of 13.5 years, and the mean length of time from 1934 to the onset of multiple sclerosis was 23.9 years, which closely approximates the currently predicted "incubation period" for the disease, Dr. Eastman noted.

The remaining six patients had moved to the town comparatively recently as adults.

"Unfortunately, it would have been almost impossible to try to find all the people who had lived in the town during those contamination episodes of 40 years ago," Dr. Eastman said.

Dr. Eastman is an intern at Beth Israel Hospital. His coauthor was Dr. David C. Poskanzer, of Massachusetts General Hospital.

Cancer Cells Held Readily Observable In Patient's Unstained Urine Sediment

Continued from page 1

can be made by radiology, cytoscopy, and biopsy, he said. The sediment examination is also useful, he added, as a follow-up on patients who have had surgery for transitional cell epithelial tumors.

Dr. Sherer cited three common characteristics of malignant transitional cells seen in unstained urinary sediment under the microscope:

- The most obvious change is in the nucleocytoplasmic ratio. The nucleus is very large and tends to crowd the cell, giving very little room for the remaining cytoplasm.
- Although unstained, the nucleus appears darker, with clumping of the nuclear protein.
- There is a great variation in the size and shape of these malignant cells.

Dr. Sherer said that the test may result in some false positives but that it nevertheless is a simple device to alert the physician to the need for further diagnostic tests.

"It is obviously better," he remarked, "to occasionally investigate a nonmalignant patient than overlook one with an early carcinoma."

Dr. Sherer, who has been using the test for one year, cited a number of cases in which suspicion of malignancy was raised by examination of the urinary sediment and confirmed by Papanicolaou smear, cystoscopy, and biopsies.

Australian Nobelist Asks to Be Spared Heroic Measures

Continued from page 1

"Since 1955 most of the advances in biomedical science have been to provide longer life to persons who neither appreciate the gift nor are capable of usefulness with it," he said. "When the old reach a stage when they cannot cope for themselves, it is true compassion to bring that intolerable stage of pre-death to an end as soon as possible."

The same holds true, he added, for babies who are genetically abnormal.

"Is there any intelligent person who, when he sees death come to someone who has been deprived of normal activity for months or years, is not impressed *with* the uselessness of having kept that person alive all that time?" he asked.

He urged "dignity in death" instead of a uselessly prolonged old age.

Sir Macfarlane is also against the prolongation of life by heart transplants. Although "mercy killing" is not socially or legally acceptable at this time, doctors should place comfort and self-respect before length of survival as objectives in treating patients who cannot look forward to an acceptable continuation of life, he declared.

In Consultation

Continued from page 5

taken quite seriously, especially if it is of such severity that usual activities, like school and friendships, are interfered with. The incidence of suicide in adolescents is high and increasing.

The physician should first assess the degree of depression, especially whether or not sleeping and eating habits are seriously disturbed, and the extent of the patient's feelings of hopelessness and helplessness about himself. A good general rule is that if the patient is not more hopeful and cheerful by the end of the first contact, he should be considered potentially suicidal and treated as an acute emergency. Any depression that does not immediately respond, even briefly, to the physician's efforts to be helpful should be considered serious enough to seek consultation.

> *"...If the patient is not more hopeful and cheerful by the end of the first contact, he should be considered potentially suicidal..."*

I have not found antidepressant drugs useful in the treatment of acute depression in adolescent outpatients. There is a time lag before the drugs become effective. They can also contribute to a false sense of security in the physician about a quite serious symptom.

continued from page 13

Dr. Leon Resnekov: "We are fortunate here at the university. We have our own cyclotron."

Myocardial infarction deaths reduced to 8 per cent through early assessment, aggressive care—and aid from cyclotron.

diology and director of the Myocardial Infarction Research Unit, mortality there is now down to eight per cent.

"We have found it is vitally important to determine early which patients are uncomplicated and which have mild or severe complications. Once this has been determined, we intervene aggressively in the complicated cases before potential crises become irreversible.

"In other words, we believe totally in the motto: 'Forewarned is forearmed,' and the earlier the warning, the better the arming."

At Chicago, the early warning system consists of sophisticated computer processing and analysis of ECG, hemodynamic measurements, and other data, together with a newly developed method of isotopic scanning of ischemic heart tissue. As appropriate interventions are made, continuous monitoring quickly tells whether treatment is effective.

Education of the computer

"When a patient enters the emergency room and a clinical diagnosis of myocardial infarction is made or suspected, he is promptly transferred to the coronary care unit, where studies are quickly undertaken to determine whether rhythm disturbances or early signs of failure of the heart as a pump have become manifest. Patients are particularly at risk within the first 24 or 48 hours and require much more aggressive management during these early hours following the onset of symptoms."

Although monitoring the ECG signal by means of analogue to digital conversion is not a new technique, it usually involves sampling signals up to 500 times per second, a rate that is not practical for continuous on-line analysis of data, so, said Dr. Resnekov, "what Dr. Fozzard and his team did, in essence, was to furnish the computer with a caricature of the ECG, instructing it to ignore nonessential data and focus on diagnostically relevant information."

This program, arbitrarily called AZTEC, eliminates unimportant detail in the signal by means of a series of processors, each reducing the data rate. A small, fast-response digital computer —the PDP-81—analyzes the ECG beat-to-beat, sampling the signal only 20 times per second.

By means of a linear interpolator, AZTEC converts the signals into a set of lines. Each set represents an average duration and voltage, and uses only two 12-bit words in memory (see Fig. 1).

In the next step, these sets of lines are converted into slopes, each of which requires only two words in memory. The result is an ordered set of lines and slopes which are available for detailed analysis and are easily stored.

A separate program recognizes muscle noise and baseline drift. It classifies the signal variously as: not analyzable; noisy, but adequate for limited analysis; quiet, available for complete analysis. This program recognizes the QRS complex, codes its shape, measures its duration and the length of the previous cycle, and takes note of the repolarization process so as to avoid confusion with other parts of the signal.

After these preliminary measurements are made, each cycle is diagnosed for basic rhythm and rate, and for premature atrial, junctional, or ventricular beats. Additional measurements then recognize and code the shape of the ST segment and the polarity and height of the QT interval and the T wave.

The computer analyzes these data on line and stores them. Information can be displayed on an oscilloscope or teleprinter, or two-dimensional histograms can be derived from the cycle-processor output (see Figs. 2 and 3), or a graph can be presented of the basic heart rate versus number of premature beats over a previous six-hour period.

All of the seven beds in the C.C.U. can be monitored in this way, and, additionally, two beds can be monitored hemodynamically.

Computer as monitor

"A patient's troubles are not entirely over after the usual three-day period in the unit (although complicated patients are retained there until they are stabilized)", says Dr. Resnekov. "There is a secondary rise of problems from roughly day 14 through day 18, so we believe patients should be monitored, although not necessarily in the coronary care unit, until they are beyond this critical point. We can also monitor in an intermediate care area, and even later on, if it proves necessary."

Because of the computer's storage and retrieval capacity, it can be asked questions, such as, What has happened to a patient over the preceding three or six hours? This flexibility is important, because it permits the physician to learn very quickly whether treatment is being effective.

"After rhythm disturbances, the heart's failing as a pump is the second major problem we must deal with. Hemodynamic measurements are important indicators of such failure, but they involve complex and time-consuming calculations. Again we turned to a computer for help—this time, to the PDP-12, a small, general purpose, high-speed digital computer."

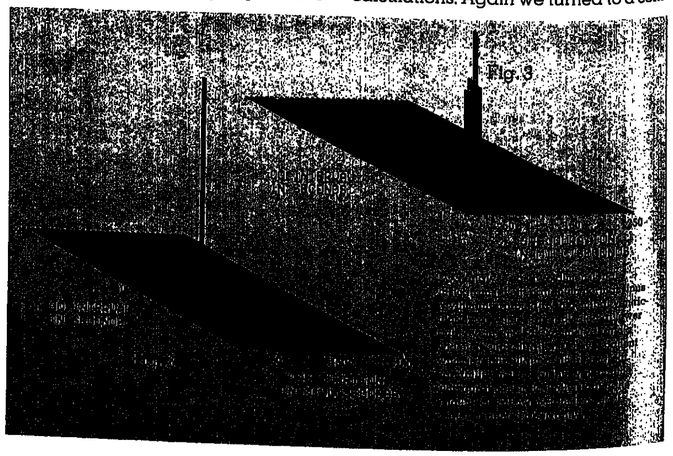


Fig. 3

With the PDP-12, the research unit can analyze hemodynamic measurements from studies in the unit or elsewhere. The program analyzes pressure and flow on line. Data are collected on multichannel FM analogue tape and edited. Selected portions are then converted to binary data. From the central arterial pressure wave the computer calculates stroke volume, heart rate, cardiac output, mean pressure, duration of systole, peripheral resistance, and systolic and diastolic pressures. It can also analyze, in the same way, arterial, ventricular, and atrial pressure pulses. The program is now being extended for use on a PDP-11 computer for on-line analysis in a new cardiac catheterization lab.

Third warning procedure

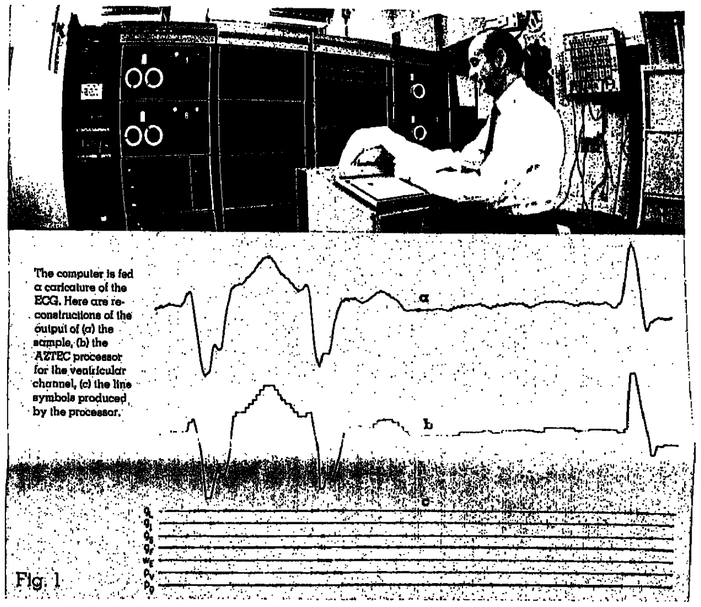
The PDP-12 also uses a conversational program to generate and store all histories. It collects information from physicians and patients in a standardized form, and investigational results are entered sequentially. It promises to be an invaluable research tool, but it is also a clinical instrument.

"If we have a patient with a particular complication," Dr. Resnekov explains, "we can ask the PDP-12 to look back and tell us how many such patients we have had to deal with in the past, what forms of treatment were most effective, and what the likely prognosis is."

The third early warning procedure developed by the research unit came out of nuclear medicine, a means to determine whether the heart is going to fail as a pump because of the size of an infarcted area.

"There is very little we can do about an area of dead heart muscle, but it is possible to make some interventions to the surrounding ischemic area. What we needed was a way to define the actual size of the damaged area, and for that we turned to our nuclear medicine people."

The nuclear department found that radioactive ammonia ($^{13}NH_4$) localized well in the heart muscle, and posed no radiation hazard because of its 20-minute half-life and the low dosage of 10 to 30 millicuries needed for a single scan. Isotopic scanning is done in the unit itself, because the Nuclear Chicago HP Anger Camera is mobile, as is its data-storage and retrieval system.



The computer is fed a caricature of the ECG. Here are reconstructions of the output of (a) the sample, (b) the AZTEC processor for the ventricular channel, (c) the line symbols produced by the processor.

Fig. 1

"We are fortunate here at the university," Dr. Resnekov admits. "We have our own cyclotron. It would be impossible to store supplies of a radioactive material with so short a half-life. But here, we make our own supplies. Then all we need is some fleet-footed person from nuclear medicine to bring the material here to the unit, where we inject it intravenously and do the scanning on the spot."

If the infarcted area proves to be extensive the patient may go into heart failure or cardiogenic shock. The first approach is the use of drugs. If that proves ineffective, a form of noninvasive circulatory support is tried. The equipment consists of a plastic box encasing a water-filled bladder, which covers the patient's legs from upper thigh to ankle. Piston-driven hydraulic pressure is applied during diastole. Arterial blood is forced back up the aorta toward the heart and down into the coronary arteries.

"This helps to perfuse ischemic heart tissue, but it also has another advantage. When the heart contracts, during systole, it does so against less resistance. Therefore we are also resting the heart."

Dr. Resnekov reports that this noninvasive circulatory support system, still experimental, improves cardiac function dramatically.

Some patients require invasive circulatory assistance, the most common being the insertion of a counter-pulsating balloon in the aorta.

"This invasive technique has one important advantage, particularly useful for the very ill patient. It can help him undergo selective coronary arteriography at this time, to determine whether direct coronary arterial surgery, with or without infarctectomy, should be done as an emergency procedure." □

report from the Roche Institute of Molecular Biology

Bacterial Transport Mechanisms

Kaback, H. Ronald, M.D.
Lombardi, Frank J., Ph.D.
Reeves, John P., Ph.D.
Short, Steven A., Ph.D.
Walsh, Christopher T., Ph.D.*
* [illegible]

Cytoplasmic membranes from a number of bacterial species spontaneously form closed vesicles, the diameters of which vary from approximately 0.2 to 1 micron (Figs. 1 and 2). These vesicles have the remarkable property of being able to concentrate solutes [e.g., sugars, amino acids, hydroxy- and dicarboxylic acids, and potassium (in the presence of the ionophore valinomycin)] in much the same way as intact bacteria. Two distinct enzymatic mechanisms have been implicated in each of these active transport systems.

One mechanism, known as "classic" active transport, catalyzes the concentration of solute against a gradient in a form that is unchanged chemically. Active transport by this mechanism is coupled to the activity of specific enzymes (dehydrogenases) and involves electron flow from a primary dehydrogenase through a membrane-bound respiratory chain to oxygen. Although the primary dehydrogenase which drives transport may differ in various organisms (e.g., in *Escherichia coli* and *Salmonella typhimurium*, D-lactate dehydrogenase drives transport, while in *Staphylococcus aureus*, α-glycerol phosphate dehydrogenase performs a similar function), the general mechanism appears to be similar in each of the vesicle systems studied. The energy-coupling site for transport is located in a segment of the respiratory chain between the primary dehydrogenase and the cytochrome chain, and the transport process may involve cyclic oxidation-reduction of critical sulfhydryl moieties in membrane-bound protein molecules which act as transmembrane "carriers."

A second type of mechanism, classified generally as a group translocation mechanism, catalyzes the vectorial phosphorylation of certain sugars (e.g., in *Escherichia coli*, glucose, fructose, mannose, sorbitol, and mannitol). The enzyme system which mediates this type of transport is known as the phosphoenolpyruvate-phosphotransferase system (abbreviated PTS). It requires at least three proteins and exhibits a requirement for a specific phospholipid (phosphatidylglycerol). Phosphate is transferred from phosphoenolpyruvate to a small molecular weight, heat-stable protein designated "HPr" [illegible] enzyme I". Phosphate is then transferred from phospho-HPr to sugar in a reaction catalyzed by a membrane-bound, sugar-specific enzyme designated "enzyme II". Studies with both isolated membrane vesicles and whole cells demonstrate that sugars are translocated across the membrane as a result of phosphorylation by this coupled enzyme system. Thus far, this type of mechanism has not been demonstrated in any organism phylogenetically higher than a bacterium.

Specific inactivators of these transport systems (i.e., D-lactate dehydrogenase in *E. coli* and *S. typhimurium* or the PTS) would yield valuable information on the physiology of these transport mechanisms. Moreover, since the PTS apparently occurs in certain bacterial species only, the possibility exists that the respiration-linked transport systems are also specific for bacterial systems. Should this be the case, inactivators of either or both of these transport mechanisms would be of considerable use as antibacterial agents in a therapeutic sense. For example, the acetylenic hydroxy acid, 2-hydroxy-3-butynoic acid, has recently been shown to behave as a "suicide" substrate for D- and L-lactate dehydrogenases in *E. coli*. These flavin-linked dehydrogenases apparently transform this compound to a carbanion intermediate which then undergoes a rearrangement to a reactive allene which, in turn, reacts with flavin adenine dinucleotide at the active site of these enzymes. Inactivation is highly specific as evidenced by the observations that other dehydrogenases are not inactivated and transport can be driven by artificial electron donor systems in an unaltered fashion. Prior to inactivation, D- and L-lactate dehydrogenases undergo 15 to 30 turnovers during which time, the oxidized product, 2-keto-3-butynoic acid, is made. Recent experiments demonstrate that this reaction product is a potent inactivator of the PTS in *E. coli*. Moreover, vinylglycolate (2-hydroxy-3-butenoic acid, the hydroxy enoic acid analogue of hydroxybutynoate), a non-activating substrate for D- and L-lactate dehydrogenases which will drive transport, is 50 to 100 times more potent.

Although a great deal remains to be done, the following observations are of considerable interest:

1) Vinylglycolate is an effective inactivator of glucose transport in whole cells and vesicles in the micromolar concentration range.

2) Vinylglycolate inhibits the growth of *E. coli* in the same micromolar concentration range.

3) Vinylglycolate treatment of *E. coli* inactivates enzyme I of the PTS.

4) Vinylglycolate is transported by a respiration-linked transport system which is specific for D- and L-lactate, and is subsequently oxidized to a keto enoic acid by membrane-bound, flavin-linked D- and L-lactate dehydrogenases.

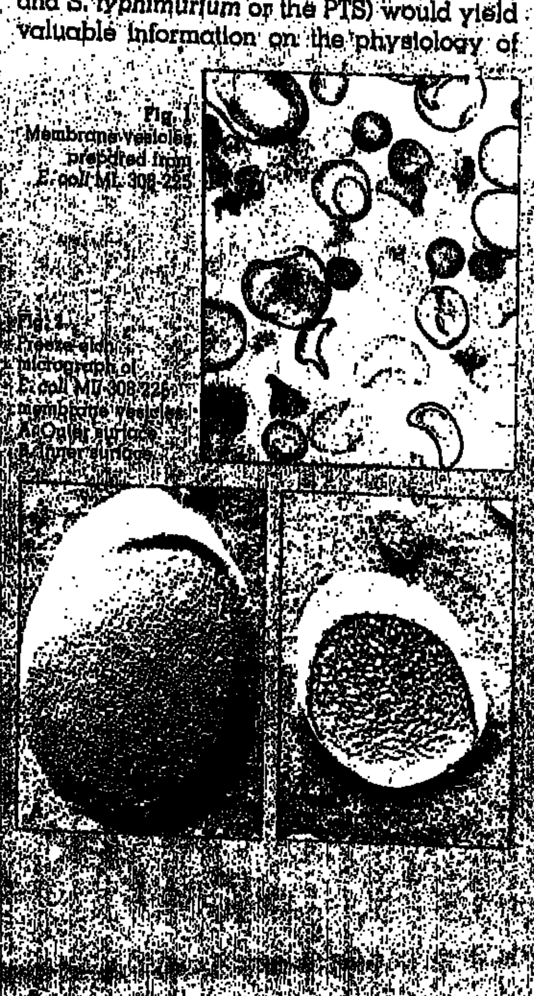
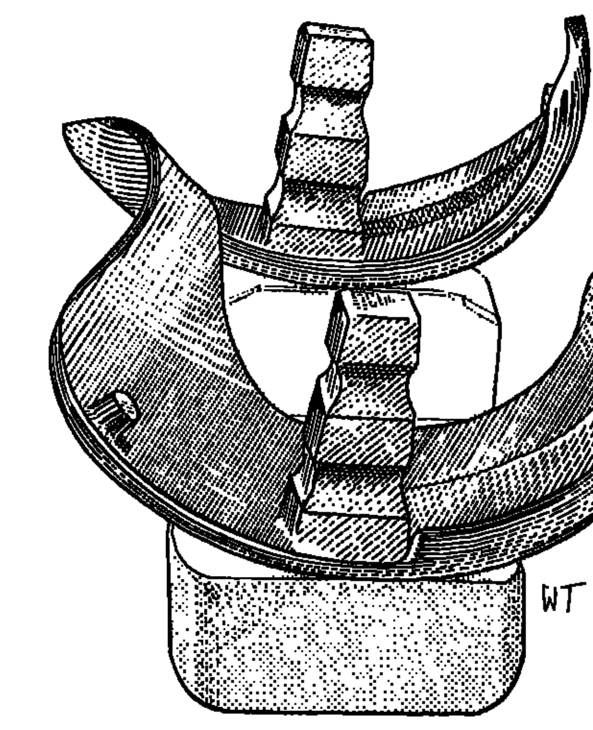
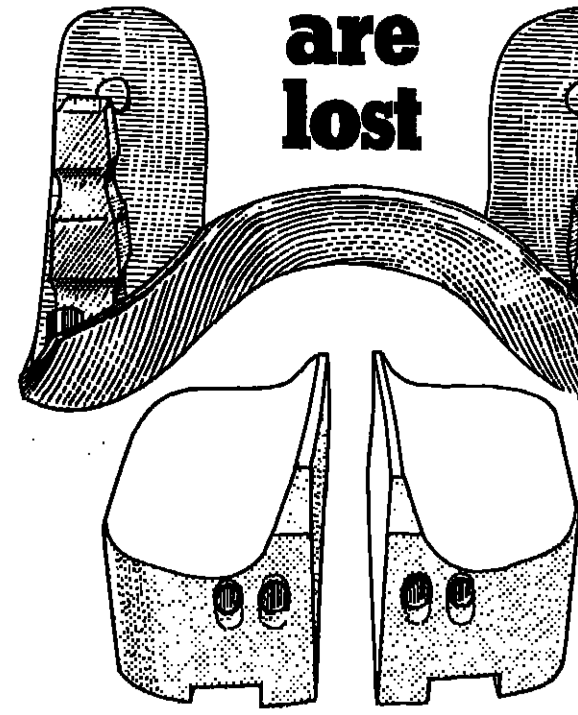


Fig. [illegible] Membrane vesicles prepared from E. coli ML 308 [illegible]

ARTHRITIC KNEE PROSTHESIS

When cartilage and bone are lost





Drawing of knee prosthesis, the Hospital for Special Surgery.

A "last resort" implant procedure, still experimental, is working well after a year in severely disabled patients.

THE KNEE JOINT would appear to be a hinge, but in fact it moves in three planes, namely, flexion-extension, adduction-abduction and axial rotation. A prosthesis that enables these motions has been developed by an engineer, Dr. Peter Walker, of the Hospital for Special Surgery, New York, in collaboration with Drs. Chitranjan S. Ranawat and John Insall of the hospital staff. It is based on a concept of condylar replacement introduced by Dr. Frank Gunston of Winnipeg, Canada. This prosthesis has been successfully used in 50 patients over the last two years.

The duo-condylar prosthesis of the Hospital for Special Surgery has a metal femoral component of cobalt-chromium or stainless steel. This has two weight-bearing surfaces for the medial and lateral condyles. They are joined anteriorly by a bar that makes insertion easier and provides another point for cement fixation in addition to the two pillars.

The weight-bearing surface of the prosthesis resembles the natural contour of the femur and, therefore, applies physiological stress to the cement-bone bond. This also allows range of motion which is quite similar to the normal polycentric pattern (characterized by variable instant centers), and insures stability throughout the arc of motion. The stability is primarily provided by the ligaments and capsule of the knee joint.

The tibial component, of high molecular weight polyethelene, has a weight-bearing surface curving upward toward the intercondylar area that provides medial-lateral and rotary stability. The under surface has a dovetail pattern for securing it with cement. They come in variable heights.

A uni-condylar version is being used when arthritis has attacked only half the knee joint. The duo-condylar prosthesis is indicated for panarthritis of the knee joint, with or without instability.

With use of the duo-condylar prosthesis, most significant improvement was noted in the relief of pain. According to Dr. Ranawat, "Pain relief is quite dramatic because the weight-bearing portion of the knee joint is replaced with artificial surfaces and stability of the joint is improved. Yet some pain could be expected from the patello-femoral joint, especially going up and down stairs or moving the joint through an arc of motion against resistance."

With increasing experience in the technique of operation, it is becoming possible to achieve a range of motion of 90° and more in the majority of the cases. The knee is stable through this arc of motion in both anteroposterior and medial-lateral planes. It is not possible to restore normal stability, but quite close to it, in all cases. Flexion deformities up to 25° can be corrected to neutral alignment.

The possible complications

Early experience has been encouraging but complications are possible, namely, wear of tibial plateau, loosening of the cement-bone bond, and—most important—delayed deep infection. "No signs of these hazards are evident thus far. To what extent they may crop up, only longer experience will tell."

If infection does occur, the salvage procedure would be an arthrodesis. That is possible because the amount of bone resected for condylar replacement is small, and infection would not spread into the medullary canal. This occurs with a hinge replacement.

"Also, wear of the plastic component may take place after long use. The surrounding tissue could react to the plastic particles thus liberated. How significant these may be in the knee joint remains to be seen."

Discussing other complications, Dr. Ranawat notes that delayed wound healing within three to six weeks after surgery is not infrequent. Occasionally, disabling patellofemoral symptoms may require patellectomy. Venous thrombosis and pulmonary embolism do occur, but less than in hip surgery.

One message to be drawn from these risks, he said, is that duo-condylar knee replacement is not for everyone.

"It is a last resort. In selecting a case, other proven methods of treatment are considered first, namely, osteotomy, arthrodesis, joint debridement, and McIntosh hemi-arthroplasty. The duo-condylar route is reserved for crippling arthritis due to degenerative joint disease, rheumatoid arthritis and traumatic arthritis.

"The success of the operation requires that deformity and instability stem primarily from the loss of cartilage and bone substance, which can be made up with prosthetic components, and that the medial, lateral and posterior cruciate ligaments be preserved. Therefore, a knee grossly unstable because of ligamentous and capsular stretching, with dislocation or marked subluxation, is not suitable for this kind of procedure. For that group, a hinge prosthesis or other kind of stabilizer—one is being developed at the Hospital for Special Surgery—is necessary." □

The documented properties of DALMANE® (flurazepam HCl) for sleep

Dalmane (flurazepam HCl) is a distinctive sleep medication—a benzodiazepine specifically indicated for insomnia. It is not a barbiturate or methaqualone, nor is it related chemically to any other available hypnotic.

The properties of Dalmane have been carefully defined and thoroughly evaluated. Results of these investigations—many of which are cited here—have documented the effectiveness and relative safety of Dalmane when the etiology of insomnia indicates need for sleep medication.

Prompt sleep induction, effective through the night[1-13]

1. Kales, A.: "Psychophysiological and Biochemical Changes Following Use and Withdrawal of Hypnotics," in Kales, A. (ed.): *Sleep: Physiology and Pathology.* Philadelphia, Lippincott, 1969, p. 331. **2.** Kales, J., *et al.: Clin. Pharmacol. Ther., 12*:691, 1971. **3.** Jacobson, A., *et al.: Psychophysiology, 7*:345, 1970. **4.** Kales, A., and Kales, J.:

Consistently effective night after night[2,3,5,6,8-13]

Little "hang-over" effect on awakening[11,14]

J.A.M.A., 213:2229, 1970. **5.** Frost, J. D., Jr.: "A System for Automatically Analyzing Sleep," Scientific Exhibit presented at Clinical Convention, A.M.A., Boston, Nov. 29-Dec. 2, 1970; and at 42nd Annual Scientific Meeting, Aerospace Med. Assoc., Houston, April 26-29, 1971. **6.** Karacan, I., *et al.*: "The Sleep Laboratory in the Investigation of Sleep and Sleep Disturbances," Scientific Exhibit presented at Amer. Psychiat. Assoc., Washington, D.C., May 3-7, 1971. **7.** Hartmann, E.: *Psychopharmacologia (Berl.), 12*:346, 1968. **8.** Dement, W. C.: Data on file, Medical Department, Hoffmann-La Roche Inc.,

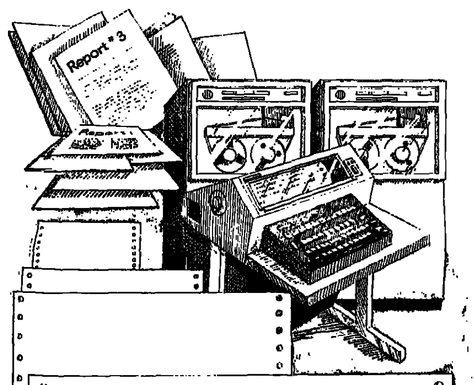
Relative safety[11,14,15*]

Nutley, N.J. **9.** Vogel, G. W.: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley, N.J. **10.** Kales, A., and Kales, J. D.: *Pharmacol. Physicians, 4*:1, 1970. **11.** Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley, N.J. **12.** Kales, A., *et al.*: *Arch. Gen. Psychiat., 23*:226, 1970. **13.** Meyer, J. A.: "Flurazepam Hydrochloride for the Short-Term Treatment of Insomnia in the

*Generally, when adverse effects were reported clinically with Dalmane (flurazepam HCl), they were mild and infrequent. Dizziness, drowsiness, lightheadedness and the like were the side effects noted most often, particularly in the elderly or debilitated. (An initial dose of Dalmane 15 mg should be prescribed for these patients.)

Usefulness in chronically anticoagulated patients[11]

Hospitalized Post-Surgical Patient," Scientific Exhibit presented at AAGP, San Francisco, Calif., Sept. 28-Oct. 1, 1970. **14.** Zimmerman, A. M.: *Curr. Ther. Res., 13*:18, 1971. **15.** Greenblatt, D., and Shader, R.: *Ann. Intern. Med., 77*:91, 1972.



Data about Dalmane (flurazepam HCl) on request

The references cited constitute only a part of the Dalmane bibliography. Additional data are available through the Roche Professional Services Department. Augmenting this service is RETRIEVE, a computer-operated data retrieval system which screens data from the published English language papers on Dalmane to help provide rapid answers to your specific questions. Coded into the computerized index are parameters that include patient age, sex, condition; product dose, side effect, frequency of administration; other medications or therapy; length, type and size of study, and pharmacology.

For specific answers to any questions you might have about Dalmane, write or call: Roche Professional Services Department, Roche Laboratories, Nutley, N.J. 07110. Telephone: (201) 235-2355.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening, in patients with recurring insomnia or poor sleeping habits, and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, diplopia, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

DALMANE®
(flurazepam HCl)
When restful sleep is indicated

One 30-mg capsule *h.s.*—usual adult dosage (15 mg may suffice in some patients).
One 15-mg capsule *h.s.*—initial dosage for elderly or debilitated patients.

ROCHE
ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Colposcopy avoids conization

Excisions of cervix uteri and its complications eliminated in 95 per cent of 2,591 women referred for abnormal cytology.

SEVEN COLPOSCOPIC clinics set up under the Wisconsin Regional Medical Program in July, 1969, have thus far examined more than 2,500 women for cervical neoplasia, and have found that conization was an unnecessary diagnostic procedure in all but a small percentage.

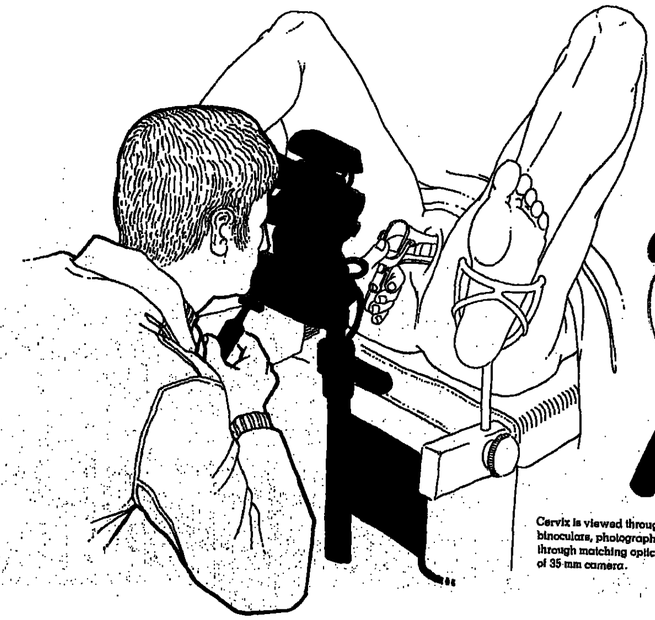
Adolf Stafl, MD, Ph.D., Department of Obstetrics and Gynecology, The Medical College of Wisconsin, reports that the need for diagnostic conization—and its attendant complications and cost—was eliminated in 95 per cent of 2,591 patients referred to the seven clinics for colposcopic evaluation of the cervix. The examinations were done by nine gynecologists previously trained as colposcopists specifically to man the clinics.

Of 2,591 patients, 2,228 were referred because of abnormal cervical cytology and 363 because of grossly suspicious cervical lesions. Diagnostic conization was performed in only 131 patients.

The need for diagnostic conization in cervical neoplasia can be substantially reduced without sacrificing diagnostic accuracy, Dr. Stafl said, when clinical colposcopy is used to complement laboratory cytology by outlining the most suspicious lesion on the cervix for a directed biopsy.

This procedure "accurately defines the histopathology of the cervical lesion in all cases in which the lesion does not extend into the endocervical canal and the entire squamocolumnar junction can be fully visualized."

Biopsy directed by colposcope avoided the cervical bleeding which frequently results from multiple punch biopsy or cervical conization, Dr. Stafl said. Avoiding conization in the pregnant patients meant avoiding an increased risk of abortion and premature delivery, and the cervical incompetence that can result from the operative procedure. And avoiding unnecessary conization of the cervix can cut the cost of diagnosing early cervical neoplasia by more than 85 per cent, because hospitalization is not required and laboratory and physician fees are reduced.



Cervix is viewed through binoculars, photographed through matching optics of 35-mm camera.

Study of technique

But Dr. Stafl cautioned that the accuracy of the method is directly related to the examiner's skill and experience with the colposcope. The use of the instrument is learned through study of color photographs of cervical lesions taken through the colposcope and subsequent hands-on work under the guidance of an experienced physician.

In Dr. Stafl's study, 179 physicians referred 2,591 patients with abnormal cytology or grossly suspicious cervical lesions for colposcopic examinations. Based on the examination, the patients were given one of three possible classifications:

• Negative colposcopy. In 913 patients the squamocolumnar junction was fully visible, but no focal colposcopic lesion was found. In the patients whose referral was based on cytology that was positive or repeatedly suspicious, conization was done in spite of the negative colposcopy in order to evaluate the false-negative rate of colposcopy, which was 1.2 per cent.

• Unsatisfatory colposcopy. In 299 patients the squamocolumnar junction was not fully visible, and a more severe lesion higher in the endocervical canal was considered possible. A diagnostic conization was recommended when the referring cytology was positive or repeatedly suspicious.

• Focal colposcopic lesion. In 1,379 patients, focal colposcopic lesions were found, and biopsies directed by colposcopic vision were performed in 1,210. In the beginning of the study, directed biopsies were performed in all patients with a focal colposcopic lesion, but the methodology was later changed and directed biopsies were deemed unnecessary in patients with "very insignificant lesions" considered "compatible with minimum histopathological changes." A diagnostic conization was necessary only when there was a major discrepancy between the diagnosis obtained through the directed biopsy and that obtained through cytology, or in cases in which the lesion extended into the endocervical canal.

Among the 2,591 patients, diagnoses by directed biopsies were as follows: invasive carcinoma, 30; microinvasive carcinoma, eight; severe dysplasia or carcinoma in situ, 352; and mild to moderate dysplasia, 574.

In the 352 cases of severe dysplasia or carcinoma in situ, diagnostic conization was required in only nine cases—those patients in whom the cervical lesion extended into the endocervical canal. In 300 of the 352, definitive surgery was performed without the need for diagnostic cervical conization. The remainder of these patients were not treated by surgical excision; some were treated by cryosurgery, some were pregnant and treatment was postponed, and two cases were lost to follow-up.

Method of evaluation

Of a total of 1,210 directed biopsies, significantly more severe changes in the surgical specimen (cone or hysterectomy) were found in five cases, so the false-negative rate of directed biopsies was .4 per cent.

In 85 per cent of the 2,591 patients, immediate treatment and disposition were based solely on the colposcopic impression and a directed biopsy.

In order to evaluate the correlation between colposcopic impressions and histopathologic diagnosis of the directed biopsy, the physician directing each biopsy recorded beforehand what he expected the cervical pathology to be.

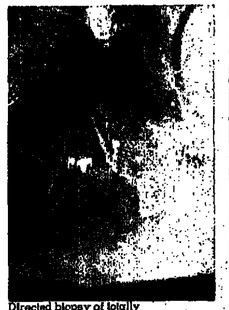
The physicians based their expectations on their observations of five morphologic features of the lesions: vascular pattern, intercapillary distance, surface pattern, color tone and clarity of demarcation.

The physicians' predictions of histopathology were clinically accurate in 86.7 per cent of the cases. The histology was less advanced than expected in 10 per cent of the cases and more advanced than expected in 3.3 per cent.

"These data correlate well with other reports in which the false-positive rate of colposcopy is relatively high," Dr. Stafl said. False-positive results are mainly due to some benign lesions (papillomas, granulation tissue) in which differentiation by colposcope from a malignant lesion becomes "extremely difficult and sometimes impossible." □

Top right, carcinoma in situ, IUD strings visible; bottom right, moderate dysplasia. Colposcope photos, U. of S. Calif. School of Medicine.

This lesion extends into the endocervical canal, requiring a conization.



Directed biopsy of totally visible lesion revealed moderate dysplasia.

LIFTING THE FOOTDROP

Electronic peroneal brace controls muscle contractions and enables stroke victim to plant foot firmly on ground.

SOMEWHERE IN PHILADELPHIA there is a sorely perplexed sneak thief. He recently entered the home of a man who had had a stroke, and whom we shall call Smith. He left with what he undoubtedly thought was a transistor radio.

It looked vaguely like one of the pocket "transistors" from which Beethoven, the Beatles, or baseball emerge, but Mr. Smith's stolen black box was nothing of the kind. It was made in Yugoslavia, not Japan. Packed with sophisticated, solid-state circuitry, it was designed to deliver a very different message through electrodes placed in an elastic stockingette located over the common peroneal nerve and deep peroneal nerve in Mr. Smith's right leg.

At the correct pulse frequency and voltage, the result of the stimulus generated by the device is a smooth contraction of Mr. Smith's peroneus longus and brevis and an overriding action of the anterolateral compartment of muscles that includes the tibialis anterior, extensor digitorum, and extensor hallucis. His right foot—which would otherwise remain flexed downward, or "dropped", the toe striking the ground in a stumbling gait—lifts as the muscles contract, enabling him to plant the foot firmly on the ground.

This may not be music to a thief, but it is to Mr. Smith, a hemiplegic stroke victim who, like most of his fellow patients, suffers from footdrop, a consequence of impaired motor function.

The device, called a functional electronic peroneal brace (FEPB), was developed at Ljubljana University by a Rehabilitation Research Program team headed by Dr. Lojze Vodovnik, a professor of electrical engineering. The research is funded under Public Law 480. Blocked dinars credited to the U.S. from the sale to Yugoslavia of surplus agricultural products are used to pay for the work.

Still in clinical trial

The device is being tested at the Krusen Center for Research and Engineering at Moss Rehabilitation Hospital, Philadelphia, by Drs. Richard Herman and F. Ray Finley. They are, respectively, director and associate director of research at the center, and Chairman and Associate Professor in the Department of Rehabilitation Medicine at Temple University. They are evaluating this and other devices for the Committee on Prosthetics Research and Development of the National Academy of Sciences.

After more than a year of study, Dr. Herman is convinced of one thing concerning the FEPB: it works, though it is not yet ready for general clinical use. Once it is perfected, however, he sees a number of advantages in its widespread use.

"Trank cosmesis as number one. Number two, the psychological barrier of having a big metal brace on the foot is eliminated. Number three, the FEPB gives you a more dynamic characteristic to the gait than you can ever obtain from present mechanical orthosis."

But there are several difficulties. "The device has not been optimized as yet. It can only be useful in about three per cent of the hemiplegic population in its present state of development. It must be upgraded, and that calls for a number of changes in the design."

He has asked the Yugoslav group to redesign the device so that it can be handled by a hemiplegic, who for all functional purposes must be regarded as one-handed, and he wants improvement in the switching mechanism which turns the device on and off in walking. Electrical configuration is the first problem.

"But the biggest problem is in the electrodes that apply the pulse to the common peroneal nerve. The existing device has its electrodes embedded in an electric stockingette pulled over the knee. The electrodes are too large, they don't conform to the contour of the body, and they are easily displaced by movement of the leg itself.

Drs. Finley (left) and Herman.

"We have long been working on the problem of how best to attach electrodes to skin. If the ideal voltage for excitation of a nerve is, say, 20 volts, one wants to get the same intensity and distribution of the current continually. Otherwise the level of contraction will vary. Variations in current are the result of coupling problems: electrodes may shift placement, or they may not adhere firmly to the skin, thereby varying the impedance and consequently the resistance offered to the applied current."

A promising answer to this problem has already been developed by the National Aeronautics and Space Administration (NASA) and applied to the concept of functional electrical stimulation by workers in the Department of Neurosurgery and Bioengineering at Temple. The answer comes in the form of an epiconductive paint.

Optimum dorsiflexion sought

"It is intended to couple with the skin *in a manner* that obviates problems created by the presence of oil, hair, and other variables on the skin. Best of all, it permits us to design an electrode that conforms to the contours of the body. We can also change the dimensions of the electrodes, trying different configurations until we find the most effective configuration for a particular patient. And of course an electrode of epiconductive paint cannot be casually dislodged or shifted by accident or by the motion of the leg."

A further reason for intensive experimentation with epiconductive paint electrodes lies in the fact that stimulation of the common peroneal nerve alone sometimes results in an outward and upward dorsiflexion of the foot, instead of straight up. By modifying the contour of the two electrodes (an anode and a cathode) near the head of the fibula, Dr. Herman and his coworkers hope to produce an optimum dorsiflexion that is neither inverted nor everted.

Patients are selected for the evaluation program by an elaborate series of neurologic, functional, and biomechanical analyses, all of which are designed to determine whether the patient fits into several models and groupings of patients that the Philadelphia investigators regard as likely to benefit. Among the criteria are: adequate hip and knee control; no sensory loss; no contracture; no marked spasticity; and fairly symmetrical loading.

Most of the approximately 50 patients using the device in this country are around 60 years of age, though some are accident victims in their teens and twenties.

By various improvements in the FEPB Dr. Herman hopes to be able to help as many as 20 per cent. The other 80 per cent are ineligible because they suffer from various disabilities not directly related to leg function per se.

"The device certainly produces in the appropriate patient a nice gait, and without the odium of an obvious orthosis, but it doesn't meet the problems of the large majority of patients. If you look at the sum of the hemiplegic's problems, footdrop is almost always one of them, but only one of many overwhelming disabilities of cortical function that affect speech, environmental perception, information processing, memory storage and retrieval, hand function, and visual-kinetic functions."

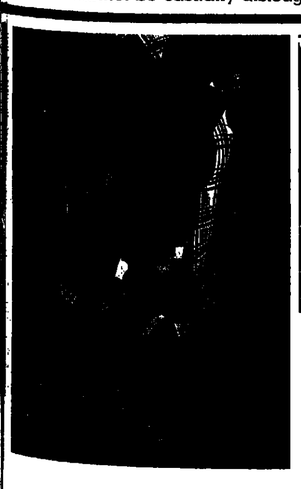
Improvements coming

Until recently, Dr. Herman, who has adopted some of NASA's turn of phrase, has kept the program in a "hold" while the Ljubljana group improves the hardware of the "black box", the footswitch, and the wiring, and the Temple group perfects the epiconductive paint. He is now testing the improved device.

He is cautiously optimistic about the future: "After all, the hearing aid, which is a sensory prosthesis, has a long history. It didn't evolve overnight. So with this device.

"Besides, physicians are traditionally careful in utilizing new techniques. They aren't going to accept even a much-improved FEPB overnight and make it routinely available to their patients. But you can be fairly sure of one thing: if it meets our standards, the government will make it available. The rest will then be up to the physicians." □

The device, complete at left, with its switch-on unit above. And to the right, model Linda Frankel demonstrates its application, adjusting electrodes in elastic stockingette, plugging the unit into inner sole, inserting that into the shoe, linking up, and finally, on her feet.



Utah Summer Plan Sends Students Into Ghetto

THE UNIVERSITY OF UTAH College of Health is once again this summer sending its students into the ghetto area of Salt Lake City to probe the emotionnl, social, and physical health problems of the poor and then make recommendations to improve the care offered. The program, started last year, sends the students off equipped with only a dime in their pockets.

Among the assigned tasks for the students was comparing prices in supermarkets and small groceries.

The students slept at the Salt Lake City Rescue Mission (above) and ate the Salvation Army dinner of a small bowl of soup and two pieces of bread (below).

One Man... and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune

'Worlds in Collision'

IN SEPTEMBER, 1949, Velikovsky wrote in his preface to *Worlds in Collision:* *"Harmony or stability in the celestial and terrestrial spheres is the point of departure of the present day concept of the world as expressed in the celestial mechanics of Newton and the theory of evolution of Darwin. If these two men of science are sacrosanct, this book is a heresy. . . ."*

"The reader is not asked to accept a theory without question. Rather, he is invited to consider for himself whether he is reading a book of fiction or nonfiction, whether what he is reading is invention or historical fact."

In brief, Velikovsky's thesis is that the Scriptures, history, and the records of different civilizations, the legends and myths from all corners of the world, contain certain common historical denominators which relate to global catastrophies—volcanic and tidal, fire and deluge, and a displacement of time. He dates these to about the middle of the second millennium before Christ and also to around 747 B.C. Velikovsky juxtaposes the Scriptures and the myths of man against geological and paleontological findings and concludes that, contrary to Newton, the cellestial arrangement with which we are familiar has not always been a totally predictable peaceful continuity but rather has been disrupted by global catastrophic events precipitated by Venus and Mars. He challenges the darwinian concept that evolution has always seen the survival of the fittest. Not being a practicing geologist, paleontologist, or astronomer, Velikovsky's efforts have been directed primarily at an analysis and synthesis of world literature, of world history as well as science. His original point of departure was the Scriptures. He has subsequently mobilized an incredible range of man's documents from tomb inscriptions to the full range of scientific literature reflecting testaments of biologists, geologists, paleontologists, and others over the centuries.

Second of series.

Velikovsky's Forerunner

Velikovsky did not claim priority for the doctrine of catastrophism. He referred on several occasions to William Whiston, 1667-1752, pupil of Newton, who published *A New Theory of the Earth*, in which he suggested that the deluge referred to in the Old Testament was caused at the end of the third millennium by a comet and that until that point in time a year consisted of 360 days and that our present year of 365 days was first introduced about the eighth century B.C.

Livio C. Stecchini quotes Whiston as follows: "Yet comets by passing through the planetary regions in all planes and directions . . . seem fit to cause vast mutations in the planets, particularly in bringing on them deluges and conflagrations, according as the planets pass through the atmosphere. . . . Indeed they do withal seem at present chaos or worlds in confusion . . . but these conjectures are left to further enquiry, when it pleases the divine providence to afford us more light about them."

Dismissal for Heresy

Whiston, who had been a temporary substitute for Newton at Cambridge, was supported by Edmond Halley, who had himself read a paper before the Royal Society a year and a half before Whiston's book, in which he explained the deluge on a cometary basis. Halley had not published his report "lest by some unguarded expression he might incur the censure of the sacred order." Whiston's recognition, for his genius and his pains, was dismissal because of heresy and trial before the body of bishops of the Church of England, a fate which society apparently reserves for those in science who have the temerity to challenge the status quo.

Velikovsky also credited Cuvier (1769-1832), founder of vertebrate paleontology, who suspected "that nature has also had her intestine scars and the globe has been broken up by revolution and catastrophies."

For almost 100 years scientists have accepted as an established "truth" the theory of evolution. Even as its origins may be traced to Aristotle, some of its elements were the teaching of Lamarck. Its fullest elaboration and popularization was by Darwin, whose name it placed in the firmament of the "stars" of science.

". . . Repeated Irruptions . . ."

Since Darwin, we tended to forget that Cuvier and others noted that "repeated irruptions and retreats of the sea have neither all been slow nor gradual; on the contrary, most of the catastrophes which have occasioned them have been sudden; and this is especially easy to be proved with regard to the last of these catastrophes, that which, by a twofold motion, has inundated, and afterwards laid dry, our present continents, or at lonst a part of the land which forms them at the present day."

As to the biblical story of the Exodus, the plagues of Egypt, the parting of the Red Sea, manna from heaven, later the walls of Jericho, and the "standing still of the sun," Velikovsky suggests that these events were not the isolated legends of one people but are reflected in the records or the myths of many and widely scattered peoples. He quotes and disagrees with Spinoza "that nature preserves a fixed and unchangeable order." He holds that "the words of Isaiah and of other seers and penmen of the Old Testament do not leave any room for doubt that by 'stones falling from the sky' were meant meteorites; by brimstone and pitch were meant brimstone and pitch; by scorching blast of fire was meant scorching blast of fire; by storm and tempest, storm and tempest; by a darkened sun, by the earth removed from its place, by change of time and seasons, were meant just these changes in the regular processes of nature."

The Reflections of Myths

He disagrees that there is "sure knowledge" and points to the fact that prior to 1803 the Academy of Sciences of Paris refused to believe that stones could fall from the sky, which possibly was endorsed by the French Academy of Sciences as a reality only following a study of a shower of meteorites on April 26, 1803. He raises fascinating questions as to mythology. Why were Jupiter, Mars, and Venus such major figures in the pantheon of the gods? He insists that mythology reflected what was at some point in time an aspect of man's real experience—an experience of such dimensions as to have impressed itself on the minds and beliefs of men for millenniums. And so he went from ambrosia to manna; from Deluge to Exodus; from mythology to man's calendars. And from these, as will be seen, he prognosticated events, bringing us into the age of Mariner and Apollo missions. But more on that later.

To be continued.

Psychiatry and Medicine

"In the last three-quarters of a century the scientific study of personality has generated a theoretical and clinical dynamic psychiatry. . . . But unfortunately **the elaboration of psychiatry as a specialty has not brought modern scientific psychiatry any closer to general medicine.** This is reflected in the traditional curricula for medical students. Psychiatry is presented as a series of separate courses and clerkships. The prospective physician rarely sees the psychiatrist on medical, surgical, pediatric, or other inpatient and outpatient services."

Greater integration is particularly important because "general medicine is undecided about the balance between scientific technology and humanism, or between patient care and social action. Psychiatry will more constructively influence the coming social evolution of medicine" if this gap is closed.

Furthermore, "if psychiatry is to live up to its capacity for instilling humanistic values in the physician—to prepare him for empathy, rapport, and sensitivity with patients and to integrate the physical and psychosocial studies of man—then it must work with the emerging physician. It must speak to the physician in terms he can understand by offering a humanistic, interhuman perspective on patients as a complement to the technological preoccupations of our modern scientific medicine." Robert E. Becker, M.D., editorial. *(Amer. J. Psychiat. 130:587, May, 1973.)*

Menu of Experts

"What is a person to eat when all of the basic food types, carbohydrate, protein and fat, have been found to have harmful effects in certain individuals. Everybody knows now that saturated fats produce high cholesterol. . . . which accelerates hardening of the arteries. . . . Protein rich foods increase purines and pyrimidines which are metabolized to uric acid which exacerbates gouty arthritis. Some of us know and more are learning that the basic carbohydrates like bread and potatoes can increase serum triglycerides in certain predisposed individuals and perhaps this too contributes to arteriosclerosis.

". . . Coffee and tea are out because they are cortical stimulants, increase heart rate, blood pressure and stimulate catecholamine release. . . .

"To paraphrase a famous quotation, **'When experts differ the public may choose.' When doctors differ regarding nutritional needs . . . the patient may choose."** Editorial. *(W. Va. Med. J. 69:128, May, 1973.)*

Easing the Manpower Lag

With today's manpower shortage in health services, it is important to set priorities and concentrate on expansion that will provide the maximal medical services at the minimal demand on personnel. Among such areas are the central service functions. **Medicine's central service functions are an important prerequisite for maximal function of both hospitals and general practitioners.** A surgical department without the possibility for carrying on clinical laboratory service and x-ray diagnostics is today unthinkable, as is a modern internal medicine clinic without a central laboratory. With relatively few doctors, a pathology-anatomy laboratory can elevate the diagnostic level and ease the daily work load for many hospitals, and serve the general practitioner within a radius of at least 200,000 inhabitants. Thus, in a time of doctor shortage it can be a good investment to go in for the expansion of vital central service laboratories. We can expect there to be a considerable need for specialists in pathology in the years to come, and that it will be difficult to find enough prospects. Olav Hilmar Iversen, editorial. *(Tidsskrift for den Norske Laegeforening [J. Norwegian M.A.] 93:7, March 10, 1973.)*

Aberrant Chromosome Traced to Genetic Shift

RESEARCH

Medical Tribune Report

ATLANTIC CITY, N.J.—The odd "Philadelphia chromosome" that crops up in bone marrow cell preparations from chronic myelogenous leukemia patients is beginning to look—by new staining techniques—like the result of a translocation of genetic material.

Dr. Janet D. Rowley of Chicago told the **American Society for Clinical Investigation** that, while positive identification is not yet complete, the Ph[1] chromosome appears to be "a truncated chromosome 22."

In addition, she said, the amount and appearance of the material that would have to be deleted from chromosome 22 to turn it into a Ph[1] is very much like the extra material that she found on the long arm of chromosome 9 in CML patients.

Dr. Rowley's findings actually occurred in the reverse order—first seeing the aberrant chromosome (called a 9q+ in the trade), tentatively identifying the added material as being of a pattern usually seen on the long arm of chromosome 22, and then hypothesizing that it had been translocated from the latter to the former.

Provisional identification of the chromosomal bits was enabled by two staining techniques that have been developed in the past few years—quinacrine fluorescence and a Giemsa stain method.

All of 20 CML patients examined by Dr. Rowley had the 9q+ chromosome, which was "seen early and persisted." Quinacrine fluorescence showed the extra material as a "dull band," and Giemsa staining picked it up as a "faint band" at the end of the long arm of the same number 9. It was from the same preparations that she determined that the added material on chromosome 9 looked like the terminal two-thirds of a chromosome 22 long arm. Further, the "plus" on the 9q was of about the same amount that, if added to the Ph[1] chromosome, would be needed to fill out a decent-appearing number 22.

CML patients in blast crisis frequently turned up more chromosomal abnormalities than Ph[1] and 9q+, Dr. Rowley said. These included the appearance of a second Ph[1], a shade different in pattern from the one seen before blast crisis; additional C-group chromosomes (which include numbers 6 through 12), a few of which resembled chromosome 8; and an occasional metacentric marker chromosome that seemed to have at least one arm that resembled the long arm of chromosome 17.

Dr. Rowley thinks that her karyotypes of CML patients begin to indicate an answer to the question that arose in 1960 with the discovery of the Ph[1] chromosome: Was the missing genetic material translocated or lost? If it is a matter of translocation specifically from 22 to 9, she said, "then that specificity is of crucial importance; when the mechanism is determined, we will have made an advance in the mechanism of carcinogenesis."

New Role for Complement Seen In 'Reverse Endocytosis'

From New York University

► In another report here, investigators from New York University described experiments that point to a new role for complement—promotion of release of lysosomal enzymes from polymorphonuclear leukocytes by means of a secretory process that they dub "reverse endocytosis."

Treated Serum Several Ways

Dr. Ira M. Goldstein and associates used several different methods of treating serum to activate an alternative pathway of complement, which generated a low-molecular-weight component that interacted with PMNs to induce selective release of lysosomal enzymes without phagocytosis occurring.

The C' component that accomplishes this is most likely C5a, said Dr. Goldstein. Its action as a "lysosomal release factor" leaves the PMNs extensively degranulated, with their lysosome and plasma membranes fused, but with no spilling of cytoplasmic lactate dehydrogenase that would spell cell lysis.

Although the experiments were based on triggering an alternative to the classic pathway of C' activation, Dr. Goldstein said that "probably C5a from any source" would accomplish the same PMN secretion of lysosomal enzymes.

Coauthors were Drs. Melchoirre Brai, A. G. Osler, and Gerald Weissmann.

2 Kinds of Lymphocytes Tied to Different Roles In Response to Cancers

Medical Tribune Report

ATLANTIC CITY, N.J.—If scientists at M. D. Anderson Hospital and Tumor Institute, Houston, Tex., are correct in their interpretation, cancer patients may be divided into those who rely chiefly on their circulating lymphocytes to combat their tumors and those who rely on their lymph node population.

Dr. Ulo Ambus reported to a meeting of the American Association for Cancer Research here that he and his colleagues had radioactively measured the reactivity (in terms of DNA synthesis) of lymphocytes from 30 patients with melanoma, sarcoma, GI tumors, breast cancer, and squamous cell carcinomas in response to tumor antigens from their malignancies.

Responses Were Varied

In general, they found that peripheral blood lymphocytes responded more to melanoma and GI cancers; lymph node lymphocytes more actively to breast and squamous cell tumors; and sarcoma very slightly to both. Patients under 59 seemed to show greater lympr node cell activity. those in advanced stages of cancer seemed to show greater lymph node cell activity.

"This could explain conflicting reports of previous investigators as to the relative roles of the two populations," Dr. Ambus observed.

"This information may allow us to choose lymph node–destroying treatments more scientifically in the total care of individual patients," he noted.

Cooperating in the research project in Houston were Drs. Giora Mavligit, Charles M. McBride, and Evan M. Hersh.

Recipes for Sipping

Wilma King, a laboratory assistant at Stanford University School of Medicine, was on a liquid diet for a year. As a result of her own experiences with often tasteless foods, she has written *Blend and Mend*, liquid recipes.

Brains Exhibited at Cornell

These brains, being examined by Dr. Hedwig Kasprzak, are from the Wilder Brain Collection and are part of an exhibit on the history of neuroanatomy at Cornell University. The display consists of 14 brains of prominent persons, including Helen Hamilton Gardener, a women's suffrage leader whose book "Sex in Brains" was prompted by a New York neurologist's contention that a woman's brain is inferior to a man's. Ms. Gardener willed her brain to Cornell "to provide superior female brains for future research." The original collection was begun in the late 1880s to provide specimens for study and came to number 1,600 brains.

Selenium May Give Protection Against Certain Carcinomas

Medical Tribune Report

COLUMBIA, MO.—Epidemiologic studies of the effects of selenium on human cancer mortality show that in geographic areas where selenium concentration is high the cancer death rate is lower than where it is either intermediate or low, it was reported here by investigators from the Cleveland Clinic Foundation and the Cleveland Clinic Educational Foundation.

Raymond J. Shamberger, Ph.D., said that marked inhibition of carcinogen-induced mouse tumor formation by topically applied and dietary sodium selenite had been previously observed. "Because human blood selenium is greater in high selenium areas, we undertook a study to see if a statistical relationship existed between selenium distribution and human cancer mortality," he told the seventh annual conference on Trace Substances in Environmental Health sponsored by the University of Missouri.

A low selenium concentration area, he explained, is one with a forage crop concentration of selenium of 0.02 to 0.05 ppm; an intermediate area has a concentration of 0.06 to 0.10 ppm.; and a high area, 0.11 ppm. or more.

It was found, Dr. Shamberger reported, that the mean value for the cancer death rate in high selenium areas is about 127 deaths per 100,000, compared with 132 and 175, respectively, in intermediate and low selenium areas.

In studies, 17 cities with populations over 80,000 and located in high selenium areas were matched with 17 of similar size in low-selenium areas on the basis of the white age-adjusted 1959-61 expected cancer deaths. The ratio of the expected cancer deaths to the observed cancer deaths was determined for each city.

The matched cities in low- and high-selenium areas were the following:

LOW-SE AREA	HIGH-SE AREA
Chicago	Los Angeles
Bridgeport, Conn.	Atlanta, Ga.
Cincinnati	Kansas City, Mo.
Portland, Ore.	San Diego, Calif.
Fall River, Mass.	Fort Worth, Tex.
Providence, R.I.	Dallas, Tex.
Youngstown, Ohio	Oklahoma City
Dayton, Ohio	Phoenix, Ariz.
Albany, N.Y.	Denver
Worcester, Mass.	Houston, Tex.
Rochester, N.Y.	New Orleans
Allentown, Pa.	San Antonio, Tex.
Brockton, Mass.	Salt Lake City
Gary, Ind.	Tulsa, Okla.
Utica, N.Y.	Birmingham, Ala.
Toledo, Ohio	Omaha
Wilmingham, Del.	Wichita, Kans.

It was found, he said, that dietary selenium is also associated with reduced mortality from cancer at several sites, especially areas of the body concerned primarily with assimilation, digestion, and excretion.

The ratio of the observed to the expected cancer deaths in the high-selenium cities showed a marked reduction in deaths due to cancer of the pharynx, esophagus, small intestine, stomach, large intestine, rectum, bladder and urinary organs, and the kidneys.

Recent evidence, Dr. Shamberger noted, indicates that antioxidants prevent carcinogenesis, possibly, he said, by decreasing peroxidation that may enhance the attachment of the carcinogen to desoxyribonucleic acid. "Using lymphocytes in tissue culture," he reported, "we have observed that the antioxidants selenium, vitamin E, butylated hydroxytoluene (BHT), and ascorbic acid markedly decrease chromosome breakage."

He hypothesized that the decline in the gastric cancer death rate in the United States since 1930 may be related to the introduction of dietary antioxidants in cereal and antioxidant food additives and the widespread popularity of cereals since that time. Some cereals, he noted, are rich in selenium.

Protection against carcinogenesis on mouse skin, said Dr. Shamberger, seems to be due to a contact mechanism rather than a systemic effect, and he noted that the gastrointestinal epithelia is similar to skin epithelia. "Dietary antioxidants might protect against gastrointestinal cancer in the same way they protect against skin carcinogenesis," he suggested.

"The apparent protection against gastric carcinoma but not against other gastrointestinal cancer in men and animals by the organic antioxidants vitamin E, BHT, butylated hydroxyanisole, and ascorbic acid," he stated, "might be explained by the fact that most of these compounds would be absorbed by the stomach or small intestine and metabolized by the liver. They would be unavailable for a direct contact mechanism or protection along the rest of the gastrointestinal tract.

"Selenium, on the other hand, seems to protect along the entire gastrointestinal tract. Selenium, which is inorganic, is excreted in the same form."

Coauthors of the report were Stanley Tytko and Dr. Charles Willis.

Elevated Testosterone Linked With Hirsutism In Study of 88 Women

Medical Tribune Report

PHILADELPHIA—Hirsutism may be considered an early manifestation of virilism and is nearly always associated with androgen overproduction, according to studies reported here by Dr. Marvin A. Kirschner, director of medicine at Newark (N.J.) Beth Israel Medical Center.

The production rate of testosterone, which appears to be the major androgen secreted in man, was found to be elevated in 86 of 88 women with hirsutism, he told the 30th International Symposium on Current Advances in Endocrinology, sponsored by Hahnemann Medical College and Hospital.

A study of 53 of the most recent patients, grouped according to severity of the condition, demonstrated that the rate of testosterone production was associated with the degree of virilism, he said. The rate ranged from the upper limit of normal, in women with increased amounts of body hair, the mildest form of virilism, to values that are comparable with those in men, in women with temporal balding and/or deep voice.

Age of Discovery Stamps

Cayetano José Heredia y García

Cayetano José Heredia y García (1797-1861) was born in Catacaos, Peru, and in 1823 received his M.D. from San Marcos, University in Lima, where he later became Professor of Medicine. He served as surgeon-general of the Peruvian Army and as physician-in-chief at the College de la Independencia. After 1845 he devoted himself to public health and went on to found the Peruvian Medical Association and establish government district physicians.

This year marks the 150th anniversary of his graduation from medical school.

Text: Dr. Joseph Kler
Stamp: Minkus Publications, Inc., New York

Vaccine for Meningococci Looks Promising in Trials

Medical Tribune Report

SAN FRANCISCO—Preliminary tests with meningococcal group A and group C polysaccharide vaccines suggest that polyvalent vaccine for protection against the disease in infants and children will be available in the near future, a University of Connecticut investigator said here.

Dr. Martha L. Lepow reported that trials with the vaccine in 250 infants from 10 weeks to 21 months of age showed that the product is safe and produces levels of antibody that appear to be age-related.

She told a meeting of the **Society for Pediatric Research** that a precise dose-response relationship has not been established and that further work must be done to determine the optimal time and dose.

The infants were injected subcutaneously on one to three occasions with meningococcal group A or group C polysaccharides.

The antibody responses on the second and third injections, at seven or 18 months, were equivalent to the primary immunization, indicating that neither immunologic tolerance nor immunologic memory had been induced by the earlier immunization, Dr. Lepow said.

In no case were local or systemic side effects seen, she added.

Drs. Irving Goldschneider, Ronald Gold, and Emil S. Gotschlick, of the University of Connecticut and Rockefeller University, New York, collaborated in the study.

Autoimmune Reaction May Cause Postpericardiotomy Syndrome

From Cornell Medical School

► Postpericardiotomy syndrome, which occurs in 25-30 per cent of patients undergoing intrapericardial surgery, may be due to an autoimmune reaction, suggested Dr. Mary Allen Engle, of Cornell Medical School.

Heart-reactive antibody apparently has a close correlation with the syndrome, she told the meeting. The presence of the anti-heart antibody is diagnostic of the syndrome, she said, suggesting that tests for the presence of the antibody would be a practical tool to aid in diagnosis.

Dr. Engle detailed a study of 86 survivors of intrapericardial surgery, in which 30 per cent of the patients developed postpericardiotomy syndrome. Appearance of the antiheart antibody at the end of the first week coincided with the first clinical evidence of the syndrome, she commented. Clinical signs included fever, pericardial friction rub, radiologic evidence of pleural and pericardial effusion, electrocardiographic abnormalities, and an elevated white count paralleling the fever.

All of the 23 patients who developed antiheart antibodies had postpericardiotomy syndrome.

The antibody apparently is muscle-specific, Dr. Engle said, and was not found in patients with lupus erythematosus, rheumatoid arthritis, or related disorders. The precise role of the antibody is unclear, she remarked.

Drs. John McCabe, Brian Denham, Paul A. Ebert, and John B. Zabriskie, of New York Hospital-Cornell University Medical Center and the Rockefeller University, were coinvestigators.

A.C.S. Urges Congress To Restore Budget

Medical Tribune Report

WASHINGTON—The American Cancer Society has urged Congress to restore the full $640,000,000 it had authorized for cancer research and control and criticized the proposed budget of $500,000,000 for the 1974 fiscal year as inadequate to meet "the urgent needs" of fighting cancer.

In testimony presented to the House Labor-HEW Subcommittee for Appropriations, A.C.S. president Dr. Arthur G. James also made a strong plea for restoration of the cancer research and clinical training program.

Citizens Budget Offered

"It is indeed unfortunate," he said, "that in the field of cancer as well as other areas this has become a matter of disagreement, with the result that new funding has been stopped and ongoing training support programs are being phased out."

Dr. James, who is Professor of Surgery at Ohio State University, testified that the American Cancer Society offered a "citizens budget" this year "because we do not agree that the proposed budget of $500,000,000 is adequate to meet the opportunities, the urgent needs to make substantial progress toward solving the problem, or the expectations of the public."

He said that there will be about 650,000 new cancer cases in the United States this year and about 350,000 persons will die of the disease. By a similar projection, he added, about 55,000,000 Americans now alive will get cancer and about 38,000,000 will succumb to it.

The cancer problem, Dr. James said, "is immediate; it is a great social, economic, and personal problem."

Pauling Says Food Lacks Adequate Vitamin C

Continued from page 1

A. The amount you need to be in good health is very difficult to get in foods. A glass of acerola juice may contain a gram or two or three of ascorbic acid, but it is so expensive that no one can afford it, and it's not available, too. Orange juice could take, how much? It would take a 6-ounce glass per day to give you 90 mg., so that would mean 60 6-ounce glasses every day. If a person lived only on high—vitamin C foods and got all his energy from them, he could get 6 Gm. a day of vitamin C. But this wouldn't be a good diet generally. It would be hard to make a good diet of tropical fruits and vegetables. Some of the prepared foods have vitamin C added, but only in small amounts.

Q. Why do you object to possible restriction of ascorbic acid dosages in pills or capsules by Federal Government regulation?

A. There has been for some years a serious danger that this vital element would have its dosages restricted. Under previous FDA Commissioner James L. Goddard public hearings were held over a long period of time. The Government sought to restrict nonprescription vitamins to certain maximum amounts equaling daily dosages recommended by the Food and Nutrition Board of the National Research Council. If the restriction was 100 mg. per tablet, a person would have to swallow 30 tablets a day to get a 3-Gm. dose. To stop a cold or reduce its side effects, if I wanted to take 10 Gm. a day, I would have to take 100 tablets. I indicated in my book, "I think I would have as much trouble swallowing all these tablets as I have swallowing some of the statements made by the Food and Drug Administration in proposing these regulations."

Q. Your book contained some strong statements in this regard.

A. Well, the FDA has made statements which are *simply* not true, and they want *falsehoods* printed prominently on the label—for example:

Vitamins and minerals are supplied in abundant amounts by commonly available foods. Except for persons with special medical needs, there is no scientific basis for recommending routine use of dietary supplements.

Q. Are there any other points in the regulations that you object to?

A. Yes, I object to their restricting factual and educational material by prohibiting any representation or suggestion that "a dietary deficiency or threatened dietary deficiency of vitamins and/or minerals is or may be due to loss of nutritive value of food by reason of the soil on which the food is grown, or the storage, transportation, processing, and cooking of food." These facts are true. They should be widely disseminated.

Q. There have been rather sharp differences on this subject between yourself, government agencies, and scientific publications. What do you think would be a constructive approach by government agencies?

A. With vitamins I would hope that, instead of forming misinterpretable regulations as to dosages, the Government would put on an educational program. It could buy time on TV and radio and advise the public, "Calculate how much you are paying. Don't buy vitamins just on the basis of qualitative statements about the vitamin preparation. Don't allow yourself to be overcharged 10-fold or 100-fold. It is really shocking that people are taken in this way with vitamins. In general they are not taken in with beefsteak. They just stop buying it when it gets to $3 a pound, and they know that $50 a pound is outrageous. Yet they just haven't learned to check the prices of vitamins on this weight basis.

Q. What do you suggest for the most economical source of ascorbic acid?

A. I think the sensible thing is to take vitamin C in the cheapest form, and you can buy it retail for $7.50 a kilogram.

Q. What do you think the FDA should do for educational campaigns on nutrition and health besides advising on prices of vitamins?

A. For one thing, it should not forbid people to publish or learn the truth about foods. It should not be illegal to state that after three months of storage, potatoes lose half of the ascorbic acid as compared with the fresh state. There is no crime in quoting a report showing that 12 ounces of potatoes, when raw, contain 50 mg. of ascorbic acid and, when cooked and reheated for serving, lose more than nine-tenths, providing only 4 mg. of ascorbic acid. Why should it be forbidden to publicize the well-known facts that food processing, as well as cooking, storage, and transportation, destroys vitamins? Why should the government interdict or hide the truth of the malnutrition potential of mineral as well as vitamin deficiencies in foods?

Q. Do you have any other objections to governmental actions or attitudes on the subject of nutrition?

A. *Yes, I consider it incredible that the Government considers it illegal for educational advertising to state the true facts that significant sections of the population of the United States are suffering or are in danger of suffering from a dietary deficiency of vitamins or minerals.*

This statement is true because one-third of our people are poverty-stricken; they are poorly nourished, suffering dietary deficiencies not only of vitamins and minerals but also proteins as well as fats. All Americans need the money to buy food and all need good, sensible advice about nutrition and knowledge about the role of vitamins and minerals.

Q. When you say "all," are you going beyond the economically disadvantaged?

A. Yes. Affluent Americans also suffer dietary deficiencies. They have the money to buy proper diets, but cola drinks, potato chips, and hamburgers do not constitute a good diet.

Q. Why has there been so much controversy in reference to your comments on ascorbic acid and the common cold?

A. Most of the critics don't read the scientific papers, and if they do, they either take a biased view or fail to analyze the basic data.

Q. Does the same skepticism apply to the role of vitamins in mental illness?

A. Yes. An application for a grant to investigate megavitamin therapy for schizophrenia was turned down by NIH with the statement that there is no clinical evidence to support the idea that it has value in schizophrenia. This is just their belief, that there is no clinical evidence. It may very well be that the clinical evidence is not completely convincing, but I would think this would be just the reason for making the grant. Professor Robinson got the idea. He was present at the on-site visit. He got the idea from the members of the committee that they were looking for someone who would be safe to get such a grant in that he would show that megavitamins didn't have any value, and they didn't think this man was the right one.

Sometimes I think that the government committees would like to find someone who would be safe, that they could give him such a grant to show megavitamins didn't have any value and they avoid the prospects of the contrary.

Q. There has been some criticism that there is a danger of overdosage with ascorbic acid.

A. The claim that patients taking heavy doses of vitamin C develop kidney stones has never been documented. Such a statement was made in *Reader's Digest* and implied in *Medical Letter* which indicated such a possibility but did not list any data in regard to patients in whom ascorbic acid caused kidney stones. I have not been able to find a report in the medical literature of even a single person with kidney stones shown to be caused by ascorbic acid. *Consumer Reports* and *Medical Letter* have failed to produce a case.

Nutrition-Teaching Programs Suggested as FDA Measure

Continued from page 1

have indicated that vitamin C may be even more important than Dr. Pauling asserted.

Concepts widely held by physicians about food as the best source of vitamins as well as FDA efforts to restrict vitamin dosages were among the subjects discussed by Dr. Pauling in MEDICAL TRIBUNE's exclusive interview. In his comments he urged the FDA to introduce educational campaigns to teach people about nutrition and health as well as ways to obtain vitamins more cheaply. He also criticized *Medical Letter* for implying—and *Reader's Digest* for asserting—that large doses of vitamin C resulted in development of kidney stones without supplying evidence of such cases.

When it was pointed out to Dr. Pauling by MEDICAL TRIBUNE that physicians are taught that food is the best source of vitamins and that a balanced diet provides adequate supplies of vitamins, Dr. Pauling asserted that "you can't get the amounts of vitamin C you need in foods. It is essentially wrong." In his view the proper amount of vitamin C needed by most people is in the order of grams per day. This cannot be achieved easily through food.

Dr. Pauling revealed that he has switched to 6 Gm. a day after taking 3 Gm. a day for six years. "It seemed to me that my health was better with high intake," he said.

He pointed out that, even with foods very rich in vitamin C, it is virtually impossible to attain a high-level intake. Acerola juice, which might supply a gram of vitamin C, is too expensive, and any other substance would require huge amounts. "It would take a 6-ounce glass per day to give you 90 mg., so that would mean 60 6-ounce glasses every day," Dr. Pauling said. By living only on high-vitamin C foods an individual might acquire 6 Gm. of it a day, "but this wouldn't be a good diet generally," he said.

Serious efforts have been made by the FDA to restrict nonprescription vitamin C to 100-mg. tablets, Dr. Pauling said. If such restrictions became law, to check a cold or reduce its severity, according to his theory, "I would have to take 100 tablets," Dr. Pauling told MEDICAL TRIBUNE. "I indicated in my book, 'I think I would have as much trouble in swallowing all these tablets as I have swallowing some of the statements made by the Food and Drug Administration in proposing these regulations.'"

Dr. Pauling asserted in the interview that "the FDA has made statements which are simply not true," citing its claim that "there is no scientific basis for recommending routine use of dietary supplements" of vitamins. He also assailed the proposed FDA prohibition of any publicizing of the fact that there may be dietary or vitamin loss as a result of soil deficiency, storage, transportation, processing, and cooking of food. Dr. Pauling believes that such facts "should be widely disseminated" instead of restricted by the FDA. "Why should it be forbidden to publicize the well-known facts that food processing as well as cooking and storage and transportation destroy vitamins?"

Suggests Buying Airwave Time

Asked by MEDICAL TRIBUNE what constructive approach government agencies could take, Dr. Pauling urged the buying of radio and TV time to advise the public on how to buy vitamins economically. "It is really shocking that people are taken in this way with vitamins," he said. "In general, they are not taken in with beefsteak. They just stop buying it when it gets to $3 a pound, and they know that $50 a pound is outrageous. Yet they just haven't learned to check the prices of vitamins on this weight basis." He advocated buying vitamin C in its cheapest form, at $7.50 per Kg.

Affluent Americans as well as the economically disadvantaged are suffering from malnutrition and dietary deficiencies, Dr. Pauling said. "Cola drinks, potato chips, and hamburgers do not constitute a good diet," he said.

In commenting on criticism of his concept of preventing and reducing the severity of the common cold through daily vitamin C dosages ranging from 1 to 2 Gm. for most people, Dr. Pauling said that "most of the critics don't read the scientific papers, and if they do, they either take a biased view or fail to analyze the basic data."

He pointed out that the NIH turned down a grant to investigate megavitamin therapy for schizophrenia "with the statement that there is no clinical evidence to support the idea that it has value in schizophrenia." In his comment, Dr. Pauling said, "It may very well be that the clinical evidence is not completely convincing, but I would think that this would be just the reason for making the grant."

Dr. Pauling cited the comments of his colleague, Prof. Arthur B. Robinson, who concluded that the Government was looking for a "safe" investigator who would find megavitamin therapy useless.

On the possibility that overdosage with vitamin C could result in kidney stones, Dr. Pauling challenged *Medical Letter*, which first suggested this, to provide data. This claim "has never been documented" and was initially challenged in a special chapter added to *Vitamin C and the Common Cold* when that book began its mass sales in a Bantam paperback edition in December, 1971.

Next week MEDICAL TRIBUNE will publish Dr. Pauling's comments during the interview on *Medical Letter* and *Consumer Reports*, which in his view published highly distorted accounts of his work. "I thought their behavior was shocking," Dr. Pauling told MEDICAL TRIBUNE. He also discussed *Medical Letter*'s failure to publish his rebuttals, its control and nonprofit status, and the discharge of Dr. Louis Lasagna, well-known pharmacologic expert of the University of Rochester, from its Advisory Board. *Medical Letter*'s attack on Dr. Pauling's work, widely quoted by others, spearheaded attacks on it in the medical press.

If there's good reason to prescribe for psychic tension...

When, for example, reassurance and counseling on repeated visits are not enough.

Effectiveness is a good reason to consider Valium® (diazepam)

After you've decided that the tense, anxious patient can benefit from antianxiety medication, the question remains: which one?

Valium is one to consider closely. One that can help to relieve the psychic tension and anxiety. One that can minimize the patient's overreaction to stress. One that is useful when somatic complaints accompany tension and anxiety. In short, one that can work and work well to help bring the patient's symptoms under control.

Effectiveness. One good reason to consider Valium.

And should you choose to prescribe Valium, you should also keep this information in mind. It is usually well tolerated; side effects most commonly reported have been drowsiness, fatigue and ataxia. Patients taking Valium should be cautioned against operating dangerous machinery or driving.

Please turn page for a summary of product information.

Valium®
(diazepam)
2-mg, 5-mg, 10-mg tablets

ROCHE

The Car Clinic

What Aquaplaning Is and How to Avoid It

By JOHN E. McDERMOTT, M.D.

"In rain the transition from control to no control is greatly accelerated, almost instant."

—Racing Safety Journal

Words of caution to the professional race driver about to drive in the rain—yet several recent developments in the family automobile have made this warning as important to you and me as to the Mario Andrettis, the Mark Donohues, and the Unser brothers. The new wide tires so common today and the lighter compact and subcompact automobiles have made "aquaplaning" a more common highway hazard.

A car, as it moves faster through water, reaches a point where contact with the pavement is lost and aquaplaning begins. The tendency to aquaplane, which means to skim across the water's surface, depends on the speed of travel, the tire size, and the car weight. Today's wider tires and lighter cars have made it a more common road hazard. Above, the rear car hydroplanes after changing lanes on soaked asphalt.

Aquaplaning

The sudden loss of control as an automobile begins to skim across the surface of the water is aquaplaning. This hydroplane effect is the result of the tires' running on the surface of the water, no longer in contact with the road below. Any object, as it moves faster through the water, reaches a point where contact is with only the surface of the water—hydroplaning!

Normally as a tire rolls along wet pavement a squeegee effect forces the water from between tire and pavement. The water is forced both into the tread and outward to the side; the tire itself remains in contact with the pavement.

Control is lost, and aquaplaning occurs, when the tire is no longer able to force out the water to reach the pavement. This is dependent on the speed, the tire size, and the car weight. The greater the tire size, the more water to move; the lighter the car, the less weight to force out the water. Increase either or both of these factors and aquaplaning will occur at lower speeds —common highway speeds!

Belted Tire

Heralded as a major advance in safety, the belted tire is in common use today. The belted principle, particularly with the radial tire design, assures greater tire surface contact with the pavement. In a dry state the better contact with the road enhances both braking and cornering. Also for rain driving, under normal wet conditions, the wide-belted tire and belted radial tire are both satisfactory. But the design of these tires can lend to increased tendency to aquaplaning. Their greater contact surface in relation to the automobiles' weight can trap more water at ordinary highway speed. This is not to say a belted tire will perform less well under wet conditions; usually it performs much better. It is merely to say that the effect of the width of the tire and the area presented makes aquaplaning more of a serious threat. When extra-wide tires are used, the threat "widens."

Aquaplaning at low speed, 30-40 mph, is a threat when wide tires are driven with insufficient tread. Water is easily trapped in wide areas of a worn tire with no grooves to dissipate. While manufactured with water-dispensing tread patterns, most wide tires are dangerous when worn smooth. Aquaplaning without warning occurs at low speeds.

Unsafe When Wet!

Some automobiles, by virtue of their weight distribution, are more prone to aquaplaning than others. Again, the differentiation between handling—i.e., braking and cornering on wet pavement—must be separated from the factor of aquaplaning. I wish to emphasize this, as the implication that a specific car might be less responsive on wet roads than another is not the intent of this comment. It is true that one car whose wet handling, braking, and cornering is legendary has also increased tendency to aquaplane.

The front wheels, which do the steering, are more critical for control; thus front-wheel aquaplaning is more dangerous than rear. With this in mind one must suspect that front-end-light automobiles are more prone to aquaplane under any given conditions than front-heavy cars. The manufacturers' proper choice of tires can reduce this hazard. However, the use of improper tires, the use of extra wide tires, or even allowing original tires to become smooth can cause the rear engine car to be dangerous "when wet."

Technique of Aquaplaning

How do you aquaplane?

You don't!

There is no sure way to control the automobile once aquaplaning. Until the tire is again able to force its way back through the water to the road, the aquaplane will continue. Then it is critical that the tire return to the road surface at the same speed it left. Not putting on the brakes, and not even changing engine speed, is important. Even more serious, any rotation of the car that begins will continue until the force is dissipated, as all road contact is lost. The steering wheel suddenly has no resistance—the engine will race as the wheels spin free—but ther real problem is rotation. The direction of travel does not change, but all too often the car turns so that it is actually traveling sideways. Disaster strikes when the aquaplane stops.

Highway Design

If aquaplaning is to be avoided, water must not be allowed to stand in puddles on the highway. These puddles, particularly if deceptive, at high speed represent extreme hazards. Recently, as a result of a successful lawsuit over a stretch of road that claimed several lives, the interest of highway authorities has focused on potentinl hazard spots. However, most such "water hazards" are unpredictable, so that only driver awareness and auto preparedness is the answer.

Anemic Youths' Misbehavior Linked With Catecholamine

Medical Tribune Report

SAN FRANCISCO—The hyperactive pattern of behavior and impaired academic achievement found in adolescents suffering from iron deficiency anemia could be due to defective catabolism of the catecholamines, according to findings detailed at the annual meeting of the Society for Pediatric Research.

Dr. Thomas E. Webb, of the University of Pennsylvania School of Medicine, said that catecholamine levels were high in a series of adolescents suffering from iron deficiency and returned to normal with the administration of iron.

He speculated that the high concentrations associated with the iron deficiency, rather than the deficiency itself, could be responsible for the poor school performance and the behavioral problems found in adolescents with iron deficiency anemia.

Dr. Webb compared 92 anemic adolescents from a Philadelphia junior high school with 101 classmates with normal hemoglobin.

Both groups were evaluated for scholastic achievement, behavioral stability, and perceptual sensitivity.

The study showed that older anemic boys displayed progressive deterioration in performance, he reported. Evaluations by teachers showed more behavior problems, such as distractability, overactivity, negativism, and disruptiveness, in the iron deficiency group.

Examinations of visual after-image formation showed a longer period of latency in the anemic group, indicating that the neural inhibitory activity in the visual system may be involved, Dr. Webb said. He remarked that this might contribute to attentional problems.

The results of the measurements of catecholamine excretion indicated a possible underlying mechanism for the problems documented in the iron deficiency group, he concluded.

Dr. Frank Oski, of the Upstate Medical Center, Syracuse, N.Y., collaborated in the study.

Polluted Water Cleansed

Medical Tribune World Service

SENDAI, JAPAN—A fast and economical method of removing cadmium, zinc, and other toxic pollutants from industrial waste has been developed in Japan.

A preparation containing petroleum, oxygen, nitrogen, and sulfur is added to waste water, which is then aerated. The pollutants are carried off with the air bubbles. The process is reported to remove more than 90 per cent of heavy metals—almost 100 per cent in the case of cadmium—from polluted water.

Regimen Slows Hodgkin's

ATLANTIC CITY, N.J.—A regimen of combined chemotherapy and irradiation in patients with childhood and adolescent Hodgkin's disease has resulted in a high remission rate without any signs of prohibitive toxicity.

In a group of 55 patients who received this therapy at the St. Jude Children's Research Hospital, Memphis, Tenn., complete remission occurred in 96 per cent, Dr. Kirby L. Smith told the 64th annual meeting of the American Association for Cancer Research.

He conducted the study from July, 1967, to July, 1972, with 38 male and 17 female patients, ranging in age from four to 20 years, with a median age of 10.

The median duration of remission for all patients is more than 26 months, with a range of six to 59 months. Thirty patients have completed all treatment and have been off therapy a median period of more than 23 months.

Early Reducing Urged

SAN FRANCISCO—To be successful, weight reduction programs should be started before a child develops adult levels of adipose tissue cells, according to a study at Mount Sinai School of Medicine, New York.

Dr. Fredda Ginsberg-Fellner told the Society for Pediatric Research that in 18 obese children a reduction in size of adipose cells accompanied weight reduction. The number of adipose cells remained constant.

Weight loss was maintained in the 11 children who had adipose tissue cell levels below the adult values, she reported, but in the seven others, weight loss was not maintained.

The seven girls and 11 boys in the study ranged from two to 10 years in age. All had documented obesity prior to one year of age. The average degree of obesity was 189 per cent above normal weight.

The children were placed on a 400-calorie reduction diet—21 per cent protein, 45 per cent fat, and 34 per cent carbohydrate—supplemented with iron and multivitamins. At the conclusion, they were followed on diets of 1,000 to 1,200 calories for six months to four years.

Dr. Jerome L. Knittle collaborated in the study.

WHO Gets Vaccine Rights

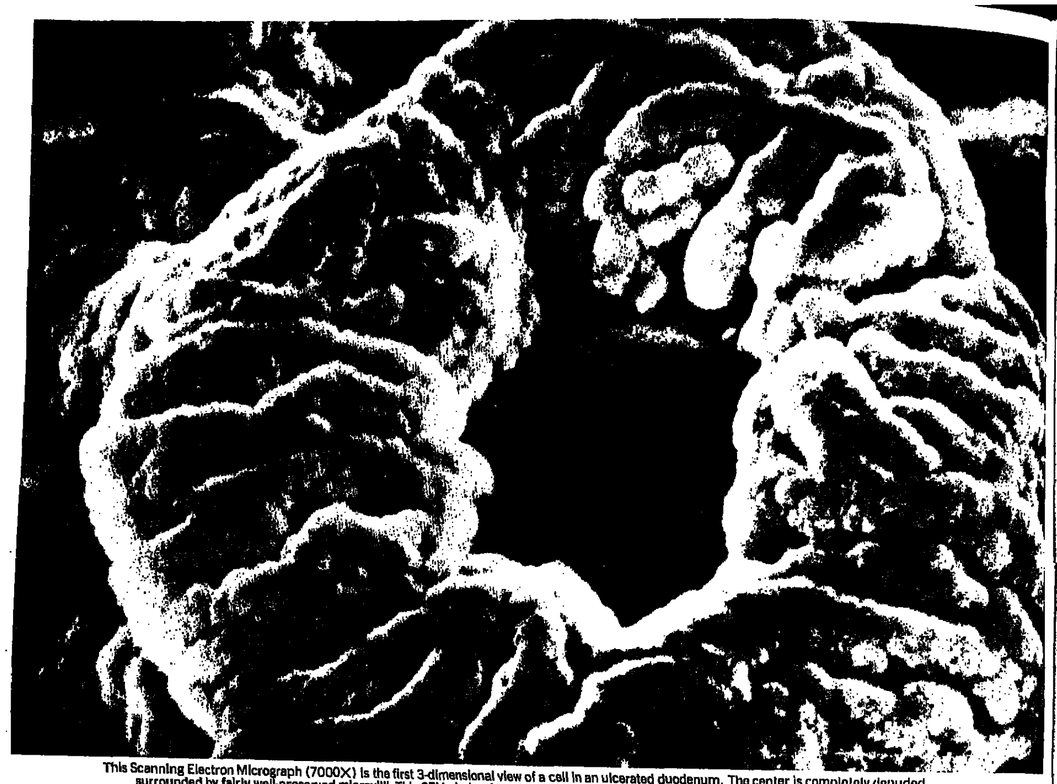
GENEVA, SWITZERLAND—Dr. Albert Sabin has transferred to the World Health Organization the right of approval for producers of his polio vaccines. Announcing this at the opening of the 26th World Health Assembly, former WHO director-general, Dr. Marcolino Candau, said the scheme would apply only to new laboratories wishing to produce vaccine from the Sabin strains for types 1, 2, and 3 polioviruses.

Until now right of approval has been exercised personally by Dr. Sabin. The new responsibility for it has been assumed by the organization, which is to set up a scientific committee to advise on all matters connected with the vaccine.

Baby Mix-Ups Increase

TOKYO—The number of babies accidentally switched in Japanese hospital maternity wards is rising as a result of lax administration and personnel shortages, a convention of legal medicine experts here was told by Dr. Suguru Akaishi, of the Tohoku University medical faculty. He cited 32 known cases of such errors in the past 15 years. Three to five known inadvertent baby swaps now take place yearly in Japan, he said, and there are indications that many more cases are going undetected.

He said that personnel and facilities have not kept pace with the rising work load. At one hospital, Dr. Akaishi noted, babies were identified only by family names.



This Scanning Electron Micrograph (7000X) is the first 3-dimensional view of a cell in an ulcerated duodenum. The center is completely denuded, surrounded by fairly well-preserved microvilli. This SEM photomicrograph was taken from a scientific exhibit which won the Hull Award as the "best exhibit on original research or instruction on a medical subject" at the A.M.A. Clinical Convention, November 26-29, 1972, in Cincinnati, Ohio.

TRIBUNE SPORTS REPORT

Throwing Injuries of Elbow Based on 2 Main Mechanisms

Medical Tribune Report

NEW YORK—Most of the throwing injuries in and about the elbow are based on medial elbow stress mechanism and shoulder whip mechanism, according to Dr. Hugh S. Tullos, Assistant Professor of Orthopedic Surgery at Baylor College of Medicine.

He told a postgraduate course on Injuries to the Neck and Upper Extremities in Sports, sponsored by the American Academy of Orthopaedic Surgeons, that both mechanisms are present in the baseball pitcher, medial stress mechanism is best visualized in the javelin thrower, and whip mechanism in the football player.

"The medial elbow stress mechanism," he explained, "begins at the termination of the cocking phase of the act of throwing. During the initiation of acceleration, the shoulder is in abduction, extension, and external rotation.

Elbow in Position of Stress

"As the ball is accelerated, the shoulder is brought forward, then the arm and the elbow. The forearm and hand are left behind. As the shoulder is whipped forward into internal rotation, the elbow is placed in a position of extreme valgus stress.

"Stabilizing the elbow against this valgus strain is the flexor forearm muscle mass. When stress on this muscle mass exceeds tissue integrity, muscular rupture can occur and has been reported rarely in adults—primarily football passers."

Avulsion fractures of the medial epicondyle, Dr. Tullos said, are more common and confined to children. The epiphysis of the growing elbow is the weaker component and stress can exceed bony integrity. The result is avulsion of the *medial epicondyle* that occurs during pitching.

In both the flexor forearm muscle rupture and the medial epicondyle avulsion the symptoms are similar—acute onset of pain with pitching, point tenderness over the lesion, and elbow flexion contracture, he noted.

In muscular rupture a palpable defect is usually present, x-rays are negative, and surgical repair is advised, Dr. Tullos said. In avulsion fractures of the medial epicondyle the lesion is usually readily identifiable on x-rays. Treatment is a posterior splint for several weeks.

"Quite unusual, but classic in javelin throwers," he observed, "is acute rupture of the medial collateral ligament of the elbow." Pain is acute in onset but less well defined than muscular rupture. The elbow is unstable to valgus stress, and this mechanism produces pain. The arthrogram is positive with extravasation of dye. "In the only case we have seen," he said, "the lesion was repaired surgically with satisfactory results."

More Common Injury Chronic

While medial elbow stress may acutely produce muscular or ligamentous rupture or bony avulsion, he noted, the more common injury, at least in adults, is chronic. Stress from throwing may result in damage to the medial elbow supporting structures. Acutely, the injury is a sprain. It is manifested by ill-defined elbow pain reproduced by stress, but no instability. Treatment is primarily rest and no throwing for six weeks.

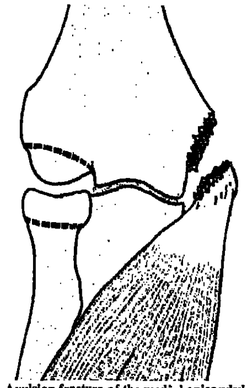
Lesions associated with the whip mechanism, as utilized by the football passer, are due to rotational stress on the humerus, Dr. Tullos said. These lesions include spontaneous fractures of the humerus in adults and stress fractures, and osteochondrosis of the proximal humeral epiphysis in children.

In the windup, or cocking phase of the pitch, the elbow is passively held in position and few problems of the elbow occur, he noted. However, one elbow lesion that does occur is the olecranon stress fracture. Here, the pathophysiology is based on the repetitive overpull of the triceps muscle.

The primary symptom of olecranon stress fractures is pain that is localized to the elbow, aggravated by pitching, and associated with point tenderness about the olecranon process. Union of the fracture can be expected with rest alone, he said.

In the follow-through phase of pitching, the arm is passive with the exception of forearm pronation, and few symptoms develop, Dr. Tullos remarked.

Javelin throwers are subject to acute rupture of the medial collateral ligament of the elbow, an otherwise unusual injury.



Avulsion fracture of the medial epicondyle is a common pitching injury among children, Dr. Tullos said. The epiphysis of the growing elbow is the weaker component and stress can exceed bony integrity.

Olecranon stress fracture is an elbow lesion that can result from repetitive overpull of a pitcher's triceps muscle.

Danes to Pay Compensation For Immunization Injuries

Medical Tribune World Service

MONTE CARLO—The new Danish law providing state compensation for persons who suffer injuries as a result of recommended or enforced immunization programs was described here at a Conference on Vaccination Against Communicable Diseases by Dr. Preben von Magnus, of Denmark's State Serum Institute.

DR. VON MAGNUS

The Danish system, recently approved by Parliament, provides compensation for economic loss due to disablement or death but does not pay for minor adverse effects of short duration, Dr. von Magnus told the conference, organized by the International Association of Biological Standardization.

The Government, however, is responsible for damages whether or not negligence can be established. The injured person is eligible for compensation provided the injury has in "reasonable probability" been caused by the inoculation. Definite proof of causal connection is not required in these cases.

The Government has the right to bring suit against the manufacturer of the vaccine.

Only persons 15 years or older are eligible for compensation, as the law is based on the loss of earnings. A child under the age of 15 is not considered to have an earning capacity. If the disability is less than 50 per cent, the benefits are usually paid in a lump sum.

Payments are also determined by age. For example, compensation for a 25-year-old with a 35 per cent disability will be about 106,000 kroner ($17,000). For a 50-year-old, it drops to 97,000 kroner ($15,000).

On disabilities that exceed 50 per cent, the Government pays annuities ranging up to 35,000 kroner ($5,500) annually. This is about 12,000 kroner ($2,000) more than payments under Denmark's Industrial Insurance Act for disabilities.

Not Necessarily Applicable Elsewhere

Dr. von Magnus suggested that the Danish law will obviate the need for costly litigation of personal injury claims connected with immunization. He also pointed out that since the law is tailored to Danish social welfare policies, it is not necessarily applicable in countries with different social welfare programs.

The Danish law places all responsibility, but also the right to recover, upon the Government. If, for example, it can be proved that there was a fault in the vaccine, it is the Government and not the individual who may sue the manufacturer. Theoretically, the right to recover any damages from a negligent physician also resides with the Government. Dr. von Magnus said he thought it highly unlikely that any such suit against the administering physician would ever arise.

IMMATERIA MEDICA

Dear Abby

Should a respectable New York typewriter of, shall we say, a certain age (which causes it to produce an unsteady line and a peculiar capital A) consent to having a blind date with a visiting typewriter from California that makes personal remarks and probably is a bit garish?

The situation began when "Immateria Medica" received a communication from Dr. Robert B. Pierce of Sacramento, Calif., occasioned by a little headline in the paper that said: "Lead Poisoning Drops."

"Where can I obtain some of these drops?" asked Dr. Pierce. We replied:

"In order to get drops with which to poison lead you must first be licensed by the FDA and then proceed through NIH channels. When you get that far, we'll send you some drops.

"In the meantime, many thanks for calling that foolish two-faced head to our attention. (Nobody here will admit to authorship.)"

Dr. Pierce soon wrote back:

"Eee Gad! You've made a terrible mistake. I don't want to poison lead at all. The lead-poisoning drops are for a patient of mine who has accidentally taken an overdose of British Anti-Lewisite. The odor is driving his wife crazy. In order to placate his wife, I feel obligated to give this man some lead poisoning drops with which to combat the accidental overdose of antidote.

"P.S. What is your typewriter on? Has it tried L-dopa instead?"

We replied, we hope with dignity:

"You'd still have to supply us with your lead poisoning licensing numbers (state and Federal) as well as the patient's social security number and MMPI score before we could consider a request for the drops. Processing of the request usually takes 11 years.

"As for the typewriter: the Smithsonian Institution is mad for it but we think we can get a million for it from the Metropolitan Museum of Art, so let's have no L-dopa-type remarks."

Well, Abby, we've heard from Dr. Pierce again:

"I regret that I was unable to comply with your suggestions which would have enabled me to obtain the lead poisoning drops, but in collecting the requisite numbers, positions, etc., I discovered that my patient has an unlisted social security number.

"A final word about your typewriter: one of our typewriters, a nostalgia freak, will be visiting in New York this summer and would like a date with your typewriter. It is absolutely incredible what will appeal to certain individuals."

So that's where it's at, and what do we do, Abby? That California typewriter might even be an electric one, for heaven's sake!

* * *

"If the total existance of the earth, as a definable planet, could be compressed into a 24-hour period, man would only have been around barely two seconds at the end of that day. The last fifty years would be represented by 0.001 second."

—Cornhusker G.P.

And that's not enough time to learn how to spell existence.

* * *

The most frightening parenthesis we've encountered in a long time turned up in a piece on telephoning in *New Scientist:*

"As the trend is toward both increased personal dialing and even longer numbers (22-digit numbers are coming soon). . . ."

Readers are invited to contribute items of 100 words or less to this column. Contributions should be mailed to MEDICAL TRIBUNE, *330 Third Avenue, New York, N.Y., 10022.*